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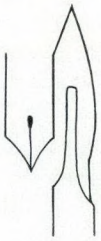

QUILL ON SCALPEL This section provides a medium through which Canadian surgeons can declare themselves, briefly and informally, on the day-to-day affairs of surgery.

CORRESPONDENCE AMONG SURGEONS

Concern about communication or the lack of it is fashionable. Although surgeons use a variety of media, the traditional scientific journal is still the most important vehicle for intramural communication. Even though many surgeons in Canada do not receive the *Canadian Journal of Surgery*, this journal still could play a significant role. Therefore, I propose certain editorial changes that would better serve the readers and those surgeons who contribute scientific articles.

How can the Journal help the practising surgeon? Surgery is a lifelong study, and after formal training ends the need for continuing education remains. We are all reminded that we need active learning rather than passive teaching. The attitudes of medical personnel and of laymen towards medicine and science and towards the scientific basis of medicine are changing even though the art of medicine, the trust of the patient and the compassion of the physician probably are timeless and not subject to change. In our present society, the relationship between those giving medical services and those receiving them is undergoing rapid and drastic changes. We have a lot to talk and write about.

At the universities, formal lectures are being replaced more and more by seminars and group discussions. In the journals, we should encourage an analogous development away from formal rigid structures; we should emphasize discussion, participation and involvement. A good paper is stimulating. Although it may rarely stimulate action, it should always stimulate thought and should often stimulate the reader to express some new point of view derived by combining an aspect of the paper with his own experience: hence, it should stimulate him to write. Writers are not born, writers are readers first. A stimulating paper will encourage them to participate in national and international discussions that could begin first in the Journal.

The full-length paper, the form most common in the *Canadian Journal of Surgery*, may not be the best for all topics. In a typical paper, the introduction presents a hypothesis, the materials and methods and results are given in detail, the hypothesis is discussed and either accepted or rejected and, finally, conclusions are drawn. A long bibliography with discussion of individual references is considered to be an asset. The reader is given sufficient detail so that, if he wants to, he can repeat the study and verify the results. If he has no intention of doing this, he may find the full-length paper boring.

There is a place for purely speculative articles, as introduced by *Lancet* a few years ago (Annotation: Hypothesis, *Lancet*, 1: 1342, 1962). Scientific articles are usually based on facts—but the interpretation of facts may be questioned. If a reader disagrees with a paper in the Journal, he should consider this an invitation to write the Editor and record his disagreement.

To further facilitate the dissemination of information which does not require a conventional paper, may I suggest the following changes: In addition to the tradi tional forms, this journal should publish "Notes" and "Communications" (terms used by the *Canadian Journal of Physiology and Pharmacology* and other journals).

A *Note*, a short paper of perhaps two to four printed pages, presents observations or results without an exhaustive bibliography and discussion. A scientist will publish the results of his main project

in a full-length paper, often after years of work. In the course of this work he will explore various avenues of approach to the main problem. Some of these may produce interesting results only indirectly related to the main topic, but suitable for a short note. The clinician could publish most of his case reports as Notes. The publication of negative results and of unsuccessful projects (clinical and experimental), in the form of short notes, should also be encouraged. A *Communication*, an even shorter paper, perhaps one to two printed pages, allows the prompt publication of important new observations, which can be followed by a complete description at a later date.

Notes and *Communications* will be subjected to the usual editorial procedures and reviews. A communication would be accepted, rejected or returned for revision promptly and, where possible, published in the next issue of the Journal. The aim of this proposed change is to establish a permanent two-way avenue of communication between all surgeons in Canada and those working in related basic sciences and other disciplines. A century ago, in Europe, some medical journals were called "*Korrespondenzblatt*". This should be our aim: correspondence among surgeons.—W. ZINGG.

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SURGERY: FASHION OR SCIENCE

In surgical practice, opinions still overwhelm fact. For centuries, the practice of medicine has been subjective. The best clinician made repeated intelligent observations, developed an impression, and established guidelines. Modern medicine goes one step further and from these observations formulates a working hypothesis as a basis for clinical investigation: it adds science to art. Hence, no physician should speak with confidence about his experiences if he has not submitted his impressions to the test. In contrast with internists, some surgeons seem to resent this approach; they seem to avoid objective studies and their practice remains empirical. As a consequence, many of our methods in clinical surgery are the subject of controversy and, in a recent editorial, Butcher[1] has accused us of scientific failure.

How could surgery be made more scientific? First, we must place less reliance on retrospective studies. Although such studies show the natural history of disease, they rarely allow us to test our hypotheses. In treatment and especially when controversy exists over different methods of treatment, we need prospective studies. Frequently, guided by impressions and without the benefit of critical assessment surgeons continue in the confidence that they have "the final answer". Indeed every few years they possess, and are in the possession of, a new "final answer". Thus it is that surgeons may change their methods from time to time and yet, throughout, declare their results excellent at all times! The evolution in the surgical management of duodenal ulcer illustrates this point beautifully. How much fruitless surgery and how much human suffering would have been avoided if controlled studies such as those of the Leeds/York group's[2] had been done and recognized earlier?

The only basic difference between a clinical prospective study and an animal experiment is one of ethical limitation. A hypothesis born of clinical impressions is tested. According to this hypothesis, some patients who fit the chosen criteria are selected and randomized. To evaluate surgical procedures, untreated controls are not necessary if the indications for operative intervention are agreed upon. The design of the study determines the type of statistical analysis and special techniques, such as sequential analysis, will reduce to a minimum the number of patients entering the study. Ideally, the clinical investigator should have a solid base in biometrics so that he can communicate effectively with the statistician who does not fully grasp all the clinical aspects of the problem. In all clinical studies, the team should decide on the statistical method before it begins to gather the results rather than try, afterwards, to find a test which gives a strong p value. Good

statistics are not a luxury. The literature is full of misleading conclusions that have appeared because basic statistical rules have been ignored.

Surgeons retreat behind all sorts of reasons to avoid controlled studies. Let us examine some of them!

(1) They may say "Most of us have had very little training in biometrics": However, in every medical centre, consultants in biostatistics are becoming increasingly available.

(2) They may say: "Our surgical training prepares us to evaluate each patient individually and we must fit the operation to his needs": However, no surgeon need enter an individual patient in a randomized study until he has evaluated the anatomical situation in the operating room.

(3) "Controlled studies are harmful to the patient": They do not have to be if the management of each test group represents an acceptable alternative; that is if both treatments under study have an equal chance of bringing benefit to the patient.

(4) They may say: "It is difficult to measure a surgical treatment because much of it depends on technical ability in contrast to medical therapy": Even though a great number of variables must be considered carefully, each procedure is a distinct form of treatment and, as such, can be tested.

In conclusion, what does objectivity have to offer? One major benefit would be fewer publications of marginal value and a decrease in the endless sterile discussions set off by these papers. At the same time, published material based on solid evidence would more quickly be recognized and the drudgery of remaining "up to date" would be reduced correspondingly. Surgery would then become a matter of science rather than fashion.—G. DEVROEDE.

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THE PEDIATRIC SURGEON'S CONSCIENCE

In pediatric surgery we occasionally perform emergency laparotomy with a provisional diagnosis of acute appendicitis, only to find neither a diseased appendix nor any other lesion. For a surgeon, this must be one of the most humbling of experiences. Presumably, we proceed with operation only after making a judgment based upon a careful analysis of all pertinent information. However, no surgeon is infallible and, hence, he cannot perform only "necessary" surgery. For this reason he should, from time to time, ask himself this question: "What can I do to keep negative explorations to a minimum?" In this respect, a distinction must be drawn between truly unnecessary operations and those procedures which, in retrospect, were unproductive but indicated.

Apart from the clinical features of the illness, what factors may influence a surgeon's decision to do an emergency appendectomy? Among the most persuasive are those that are psychologic or are related to the surgeon's own convenience. If the surgeon recently treated a child with far-advanced appendicitis who had only minimal symptoms and signs, he will broaden his criteria for operation for the next few patients. Referring doctors dropping in to "assist at surgery", or who have told the child's parents that "his appendix must come out right away" may sway a surgeon towards operation when, if left alone, he may have temporized. It is more convenient to do an appendectomy at 9 p.m. than risk having to operate at 3 a.m. or 4 a.m. after six hours' observation. Many surgeons prefer to operate on a "doubtful case" on Friday afternoon before departing on a holiday weekend, rather than leave the operation, if it proves to be necessary, to the surgeon on call for the weekend. The surgeon who accepts the responsibility of deciding that the child does not have appendicitis frequently bears a heavier responsibility and expends more time and effort than he who decides to proceed promptly with appendectomy. Unfortunately, too, he received only a fraction of the fee that he would have received had he operated at once.

In all these circumstances, intervention can be justified more or less on the principle that, because removing the normal appendix has an insignificant mortality, it is better to be certain than to take the chance that the child has appendicitis. However, unless strongly curbed, this rationale weakens one's resolve to make the rigorous analysis that should precede every decision to operate.

When operating for acute appendicitis, the surgeon who finds a normal appendix can sometimes look back and recognize features in the history and examination that, if fully appreciated, might have altered the decision to operate. Hence, the conscientious surgeon will review all such cases carefully to improve his ability to assess the acute abdomen.

Because incarcerated infantile inguinal hernias are most common in the first few months of life, most pediatric surgeons recommend herniotomy, regardless of the child's age, once the diagnosis of inguinal hernia has been made. If the surgeon cannot demonstrate herniation, but the mother describes clearly an inguinal lump that appeared when the baby cried and that she reduced manually, he probably should still proceed. However, the surgeon who repairs congenital hernias on the basis of history alone will occasionally find no abnormal patency of the processus vaginalis and hence no hernial sac. However, if the anesthetist is skilled and the surgeon injures neither cord structures nor posterior inguinal wall, no harm will have been done. In fact, most conscientious men are willing to risk complications and proceed with herniotomy if the history is sufficiently convincing. They believe that such a policy decreases the incidence of incarceration, and hence reduces the morbidity associated with infantile inguinal hernias.

The diagnosis of hypertrophic pyloric stenosis is usually straightforward and with careful appraisal even the most atypical presentations can usually be recognized. However, the surgeon who does not have the time and patience frequently necessary to palpate the pyloric tumour, will some day operate on a baby with a "typical" history whose "typical" tumour was easily felt by the referring doctor, or he may have convinced himself that the liver edge or kidney he was feeling was a pyloric tumour. Indeed at a recent meeting of the American Academy of Pediatrics, a show of hands indicated that a surprising number of pediatric surgeons found no pyloric tumour in as many as one-quarter of infants operated upon for pyloric stenosis.

When considering surgical correction of testicular malposition, the surgeon may be convinced that the child requires orchidopexy but, from time to time, may discover that after induction of anesthesia the testicle can be manipulated into the scrotum, is clearly retractile, and hence normal. Unfortunately, many such children may be operated upon without having been examined under anesthesia. These patients should always be examined carefully under anesthesia and the surgeon need make no apology when he cancels the operation on the basis of this examination. Although orchidopexy for retractile testicle gives almost certain good results, such surgery is unnecessary.

It is apparent that some seemingly unnecessary operations are indicated; for example, negative inguinal exploration when the history strongly indicates a hernia; the removal of a normal appendix when the diagnosis of appendicitis cannot be ruled out with confidence: but others cannot be justified; for example, negative exploration for hypertrophic pyloric stenosis or orchidopexy for retractile testicle. The conscientious surgeon will keep the former to a minimum and, if possible, completely avoid the latter.

Surgeons must continue to accept full responsibility for committing other human beings to operation and for any outcome of these operations. As thoughtful surgeons we must be convinced of the validity of each diagnosis and refuse to accept much on faith. Let us continue to review our indications for each operation, ensuring that, as often as possible, they are based solely on scientific considerations as befits a strict surgical conscience. In no other way can we deserve the respect of our colleagues and, most of all, of ourselves.

—J. C. FALLIS.

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RUPTURES OF THE ROTATOR CUFF: FOLLOW-UP EVALUATION OF OPERATIVE REPAIRS

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ORTHOPEDIC surgeons do not yet agree about the proper management of patients with disruption of the rotator cuff. Since Codman[1, 2] began to repair these cuff tears, Outland and Shepherd,[3] Wilson,[4] McLaughlin,[5-8] Moseley,[9-11] and Heikel[12] have reported a high percentage of good results from such surgical repair. Others advocate operative repair in all or only in selected rotator-cuff tears.[13-20] However, many tears of the rotator cuff will improve spontaneously on conservative care alone. Because in many areas a number of surgeons share the care of these patients, we have evaluated the results obtained by several different surgeons in reconstructing the rotator-cuff mechanism.

METHOD OF STUDY

Tears of the rotator cuff were repaired in 71 shoulders in 69 patients. In every case the surgeon attempted to reconstitute the ruptured cuff and restore it to full function. Several surgeons did the operations and used various procedures (Table I). All these patients were interviewed and examined by one of the authors (D.W.).

TABLE I.—PROCEDURES EMPLOYED

Group	*Procedure*	*No. of shoulders*
I	Simple approximation of the margins of the tear	9
II	Simple approximation combined with partial or complete excision of the acromion, excision of the distal end of the clavicle and/or division of the acromiohumeral ligament	21
III	I or II combined with fascial reinforcement or reinforcement with biceps tendon	6
IV	Mobilization of the torn supraspinatus and reattachment to bone	19
V	IV combined with fascial reinforcement or I or II repairs	13
VI	Supraspinatus advancement (Debeyre, Patte and Elmelik[17])	3

The average age of these patients was 54.6 years—the range was 32 to 72 years. There were 64 men and five women. The mean follow-up was 67.3 months (approximately 5½ years) with a range of three months to 9½ years. One patient was examined only three months after operation; we included him because he had already returned to his previous employment. Two patients were followed for only 10 and 11 months respectively, but all others were examined a year or more after operation.

In 49 of these cases the right shoulder was injured and in 22 the left. In 48 (68%) the dominant shoulder was affected—an important factor in relation to the patient's ability to return to work.

In 48 (68%) of the rotator-cuff tears examined, injury was due to falls on the shoulder, hand or elbow; in 15 (21%) to lifting heavy objects; and in eight (11%) to pulling a heavy object. However, the cuff may have been torn before the accident.

TABLE II.—TYPES OF TEARS

Type	*No. of cases*
Partial	1
Complete	70
Small	7
Medium	11
Large	34
Massive avulsion	18

Conventionally we have classified these tears into partial and complete, depending on whether the tear communicated with the overlying subacromial bursa. By this definition, all but one rotator-cuff tear in this series was complete. These tears have also been classified by dimension and appearance but, except for massive avulsion, the operative notes do not give an accurate description of the anatomical type and size of the tear (Table II).

Because of the difficulty of accurately defining the tear, we made no attempt to correlate the size of the tear with the final result except in 18 massive avulsions.

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Results

In these shoulders, we studied pain, motion and strength—factors that, although interrelated, were considered individually.

Pain Relief

Sufficient force applied to the normal muscle-tendon-bone system will produce an avulsion fracture of the bone.[21, 22] The tendon will rupture first only if weakened by pre-existing degenerative changes.[23] The rotator cuff ruptures only in the presence of degenerative tendinitis.

Since Codman's original paper[1] many authors have pointed out that supraspinatus tendinitis frequently gives rise to a painful shoulder, the symptoms of which usually abate within 18 months. Almost all our patients had intermittent discomfort in the affected shoulder before the accident which suggested rotator-cuff tendinitis. After the accident they had a sudden and marked increase in pain in addition to the gross limitation of movement. It must be acknowledged that some of the pain that persisted after operation may have been due to associated rotator-cuff tendinitis. It must also be acknowledged that, in some patients, the gradual relief of pain after operation may be due to a spontaneous remission of the associated tendinitis and that such relief could perhaps be obtained even when the operative repair of the defect had failed. Anderson and Moore[24] reported that, in 29 of 50 shoulders in patients who had no symptoms referable to the shoulder, they found evidence of degeneration of the inner surface of the cuff at post mortem. Wilson and Duff,[25] De Palma,[26] and Keyes[27] found rotator-cuff tears at autopsy in 20% to 40% of shoulders inspected. (It is interesting to note that De Palma[26] and Olsson[28] concluded that disability from cuff tears was not necessarily related to the size of the tear.)

In this review, in 55 cases (77%), the patient had significant relief of pain after the operative repair (Table III).

TABLE III.—Relief of Pain

Grade	
IV	Complete relief of pain (15 patients)
III	Occasional aching pain with weather changes or stress in certain positions of function (33 patients)
II	Occasional pain controlled with non-narcotic medication (7 patients)
I	Frequent aching pain necessitating frequent non-narcotic medication (13 patients)
0	Frequent pain requiring narcotic analgesics and/or local injections or continuing preoperative pain of identical intensity and frequency (3 patients)

Motion

All patients were asked to estimate the residual loss of shoulder motion at the follow-up examination. The difference between motion and strength was clearly outlined to each patient. In 56 cases (79%) the patient said the operation had not restored the original range of shoulder movement and in 25 (35%) the patient felt that the affected shoulder was grossly restricted (Table IV). This subjective assessment correlated well with the objective findings.

TABLE IV.—Motion: Subjective Results

Grade	
III	No significant loss (15 patients)
II	Minimal loss (22 patients)
I	Moderate loss (9 patients)
0	Considerable loss (25 patients)

Functionally, the reader must recall the normal activity of the cuff muscles and, in particular, the deltoid and supraspinatus, to appreciate the mechanical changes produced by a rotator-cuff tear. In concert with the supraspinatus, the deltoid is a powerful abductor. In the initial phases of abduction it is at a mechanical disadvantage and, because it pulls along the long axis of the humerus, it tends to displace the humeral head superiorly. This superior drift is counteracted by the supraspinatus, which fixes the head of the glenoid and depresses it during abduction.[29]

Normally, during abduction and forward flexion, the scapula and humerus move together. In abduction greater than 90° the scapula must rotate. These movements occur simultaneously and not successively, and the scapula rotates approximately one degree for every two degrees of glenohumeral movement.[30] The composite of these synchronous muscle contractions is generally referred to as "scapulohumeral rhythm".

Electromyographic studies confirm that the supraspinatus initiates abduction and acts with the deltoid throughout, reaching

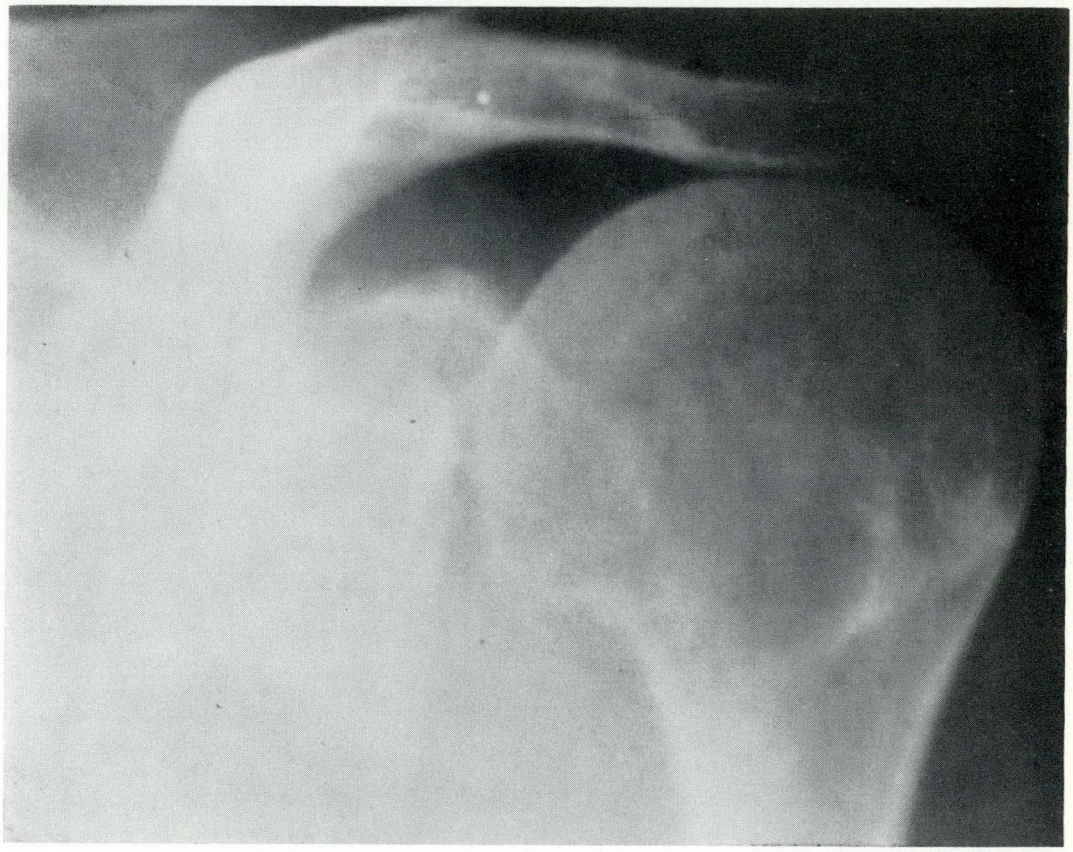

Fig. 1.—Radiograph showing upward migration of the head of the humerus in relation to the glenoid.

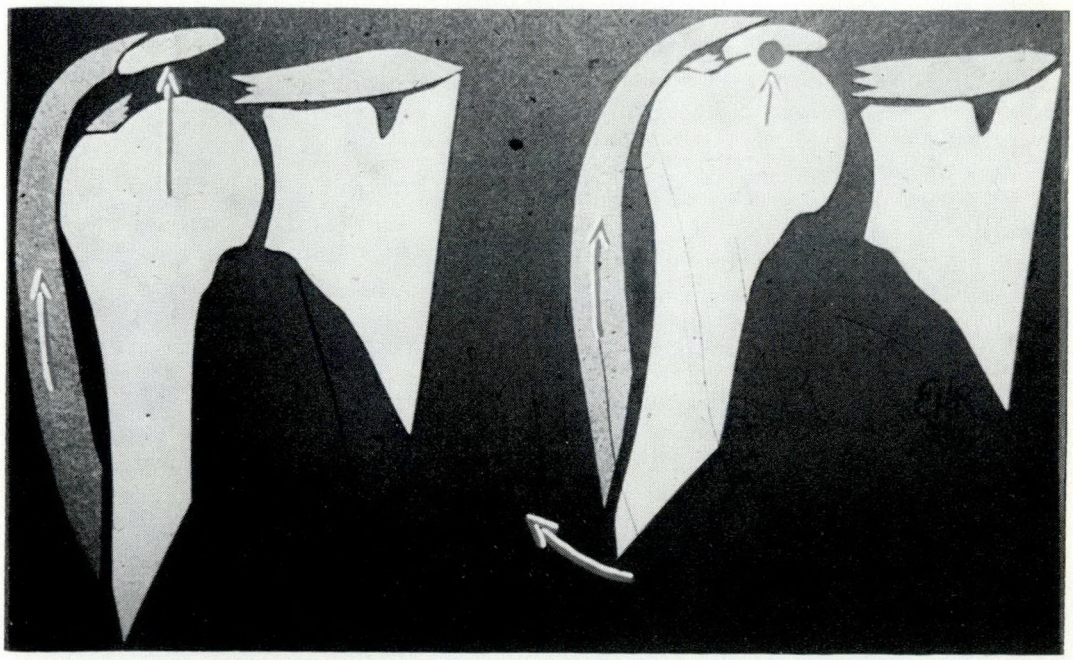

Fig. 2.—Diagram to show the acromion acting as a fulcrum of movement.

its maximum at 100° abduction.[31, 32] However, van Linge and Mulder[33] have shown that normal subjects can only reach full abduction after the suprascapular nerve has been blocked by local anesthetic. This important observation indicates that the ability to abduct the shoulder above the horizontal plane does not necessarily indicate anatomical integrity of the supraspinatus. Moreover, in untreated avulsions of the rotator cuff, the head of the humerus may migrate superiorly and eventually impinge against the undersurface of the acromion (Fig. 1).[27, 34] Here a false joint may form in which the acromion acts as a fulcrum allowing the deltoid to initiate abduction (Fig. 2).[35] These factors must be considered when assessing the result of operation.

TABLE V.—Motion: Objective Assessment

Grade	*Abduction in the scapular plane (degrees)*	*No. of cases*
V	Greater than 140	14
IV	120 – 135	17
III	100 – 115	6
II	90 – 95	16
I	60 – 85	9
0	Less than 60	9
	Forward flexion (degrees)	
V	Greater than 140	34
IV	120 – 135	10
III	100 – 115	4
II	90 – 95	8
I	60 – 85	7
0	Less than 60	8

All ranges of motion measured were combinations of glenohumeral motion and scapulothoracic rotation. Because when at work these patients use both these maneuvers to put their arms in desired positions, we did not attempt to distinguish between them. The range of motion recorded before operation was obtained from medical files, although the exact method of measurement was unknown. This unknown became important when we attempted to draw definite conclusions by comparing recorded preoperative and final ranges of motion. All final measurements were recorded with a goniometer using the midsagittal line of the trunk as the base limb of the resulting angle. For final assessment we used only the ranges of abduction in the scapular plane and forward flexion (Table V).

Only 14 patients (20%) could abduct above 140° and 18 (25%) could not reach the horizontal plane. Most patients showed a greater range of forward flexion; 34 (48%) achieved forward flexion of more than 140°, probably because in forward flexion the cuff is less likely to impinge beneath the acromion, and because additional shoulder muscles are used in forward flexion.

TABLE VI.—Strength

Grade	
IV	Complete restoration (7 patients)
III	Good restoration—weakness while working at or above the horizontal plane (21 patients)
II	Unable to work at or above the horizontal plane—satisfactory at low levels (33 patients)
I	Unable to work at either level, but able to perform activities of daily living with the involved shoulder (4 patients)
0	Unable to use the shoulder for any functional activity (6 patients)

Strength

All patients were asked to estimate the strength of the affected shoulder and we attempted to make plain to each patient the difference between strength and endurance although these two functions are closely related. Sixty-four (90%) believed that the strength of the shoulder was noticeably less than before the accident (Table VI).

In this investigation we tested the strength of shoulder movement with the shoulder abducted in the scapular plane at 90°; likewise we tested forward flexion in the 90° forward flexed position. Patients who could not reach the testing position were rated 0, and those who could maintain the testing position against strong resistance were rated IV. We also recorded intermediate grades of strength (Table VII).

Thirty-nine patients (55%) could not maintain the testing position against two-finger resistance, or could not reach the testing position for abduction. Twenty-nine patients (41%) could not maintain the testing position against two-finger resistance, or could not reach the testing position for forward flexion. Only 25 patients (35%) could maintain the testing position against strong resistance in abduction and 37 (52%) in forward flexion. In 50 of the 71 shoulders studied, failure to regain full range of movement and nor-

TABLE VII.—Strength: Objective Assessment

Grade	*Abduction*
IV	Ability to maintain the testing position against strong resistance (25 patients)
III	Ability to maintain the testing position against two-finger resistance only (7 patients)
II	Inability to maintain the testing position against two-finger resistance (21 patients)
I	Inability to maintain the testing position against gravity (none)
0	Inability to reach the testing position (18 patients)
Grade	*Forward flexion*
IV	Ability to maintain the testing position against strong resistance (37 patients)
III	Ability to maintain the testing position against two-finger resistance only (5 patients)
II	Inability to maintain the testing position against two-finger resistance (14 patients)
I	Inability to maintain the testing position against gravity (none)
0	Inability to reach the testing position (15 patients)

mal power was associated with visually apparent minimal-to-marked atrophy.

Economic Results

Seventy-nine per cent of the patients felt that they had not regained their original range of movement and, on clinical testing, only 20% could abduct above 140°. Associated with this was significant loss of strength; only 35% could maintain the shoulder in 90° abduction against strong resistance. Ninety-two per cent of these patients also felt they had a noticeable reduction in endurance. Atrophy of some degree in 70% of patients, when considered with these findings, suggests that operative repairs did not restore functional integrity in most of these patients. Despite this, 36 patients (52%) ultimately returned to their original jobs, or similar jobs, without losing significant time after their return to work (Table VIII). Fifty-five patients (80%) returned to their original jobs, or a modified job, and lost less than 20% of time after they returned. Only nine (13%) could not return to work at all, either because of premature retirement enforced by the shoulder disability, or because they could not do any work at all. All patients were asked to assess the results they had obtained in terms of the degree of function and also loss of pain and the ability to return to work without subsequent time loss. Because compensation falls far below the potential income of these patients we believe all these patients wanted to return to some form of gainful employment.

TABLE VIII.—Return to Gainful Employment

Grade	
VI	Returned to exact or identical type of employment, no significant time loss (36 patients—52%)
V	Returned to modified job due to shoulder disability, no significant time loss (13 patients—19%)
IV	Returned to modified job due to shoulder disability, less than 20% time loss (6 patients—9%)
III	Returned to modified job due to shoulder disability, 25% time loss (3 patients—4%)
II	Returned to modified job due to shoulder disability, greater than 50% time loss (2 patients—3%)
I	Shoulder status and age induced patient to retire (4 patients—6%)
0	Did not return to work because of shoulder disability (5 patients—7%)

Thirty-eight (54%) believed that they had benefited from the operation and indeed 51 (72%) were satisfied with the operative results (Table IX). The greatest improvement, however, was relief of pain —77% reported such relief. As noted above, one cannot attribute relief of pain entirely to the operation because some relief could represent spontaneous remission of associated rotator-cuff tendinitis. In addition, 24 of the 69 patients changed their occupation to one that did not involve work above shoulder level and therefore did not require complete function of the cuff mechanism. Freedom from pain and change of occupation subsequently helped many patients to take gainful employment even though they did not have full mobility and strength.

TABLE IX.—Patients' Overall Assessment

Beneficial	Under similar circumstances the patient would have the procedure again and felt that it was ultimately beneficial (38 cases)
Satisfactory	The patient would go through procedure again but felt that the result was not as beneficial as expected or desired (13 cases)
Unsatisfactory	The patients' final result was not as good as expected or desired; they would not have had the procedure if they had known the result (17 cases)
Undecided but unsatisfactory	Patients were unable to decide whether they would have the operation again. All had unsatisfactory function, but had varying relief of pain (3 patients)

Unsatisfactory Results

In investigations of this type, analysis of unsatisfactory results generally provides the most information. We eventually classified 20 shoulders as grossly unsatisfactory (Table X). In 14 of the 20 cases, the dominant extremity was involved. In their jobs all these patients had had to use the extremity at or above the horizontal plane.

TABLE X.—Analysis of Unsatisfactory Results

Case no.	Dominant side	Surgical type	Apparent size of tear	Subjective motion	Objective motion	Subjective strength	Objective strength	Pain rating	Return to work
1	Yes	II	IV	0	I	0	0	I	II
2	Yes	II	III	0	I	0	0	I	V
3	Yes	III	IV	0	0	0	0	III	V
4	Yes	IV	V	0	0	I	0	I	I
5	No	II	III	0	I	II	0	III	III
6	Yes	V	V	0	IV	I	II	III	0
7	Yes	II	II	0	II	II	IV	0	V
8	Yes	V	IV	0	0	I	0	II	0
9	No	V	V	0	III	II	II	I	III
10	Yes	IV	V	0	0	I	0	III	0
11	Yes	IV	V	0	II	II	II	III	V
12	Yes	IV	V	0	II	II	II	0	V
13	No	II	IV	0	II	II	II	I	IV
14	No	II	I	0	0	I	0	III	I
15	No	V	IV	0	0	0	0	I	0
16	Yes	II	II	0	II	I	III	I	0
17	Yes	II	IV	0	I	II	0	III	V
18	No	V	V	0	0	0	0	0	I
19	Yes	V	III	0	I	II	0	II	V
20	Yes	II	II	0	III	II	II	I	III

Roman numerals refer to the ratings used in analysis of individual factors.

None returned to their previous jobs or similar jobs. Only 8 of the 20 returned to a modified job with less than 20% subsequent time loss. In the 18 patients who had massive avulsion of the rotator cuff, seven eventually had an unsatisfactory result.

Recalling that 55 patients had significant relief from pain, it is interesting to note that 11 of the 20 patients with unsatisfactory results had frequent pain and had to use analgesics from time to time. None of those with an unsatisfactory result had complete relief of pain.

With respect to strength and motion, 12 of the 20 could not reach the testing position and five more could barely reach this position. Of three who could actively abduct to 100° or more, two did not obtain pain relief. Moreover, of eight who could reach or exceed the testing position (90° abduction), six could not sustain the position against two-finger resistance, and one could not sustain it against full resistance. The only patient who could maintain the testing position against full resistance had an unsatisfactory result because of persisting severe pain.

On appraising the unsatisfactory results, the following pattern was noted: In their normal occupation all these patients required a functional, relatively pain-free shoulder. In various combinations all failed to achieve significant pain relief, sufficient motion or sufficient strength in the involved shoulder. The most striking features were persistent pain and markedly diminished strength.

Discussion

The results obtained in these 69 patients suggest that operative repair frequently does not restore the torn rotator cuff to normal function. When assessing the reasons for this failure we must take into consideration the underlying pathologic changes. At the insertion of the supraspinatus there is a constant area of hypovascularity where degenerative changes are first seen (Fig. 3).[36] As the degeneration continues the tendon attenuates and, as a result of minor trauma, may rupture (Fig. 4).[23] The rupture, therefore, occurs in an area of degenerated avascular tendon that may be surrounded by a zone of reactive tendinitis (Fig. 5).[36] Thus, operative repair is fraught with technical difficulties and the large number of unsatisfactory results in this series raises the question as to whether any such repair should be attempted. However, a technique to restore normal functional anatomy of the disrupted tendon would prevent loss of range of active movement, strength and endurance, and would secure a better functional result. In this regard, Debeyre, Patte and

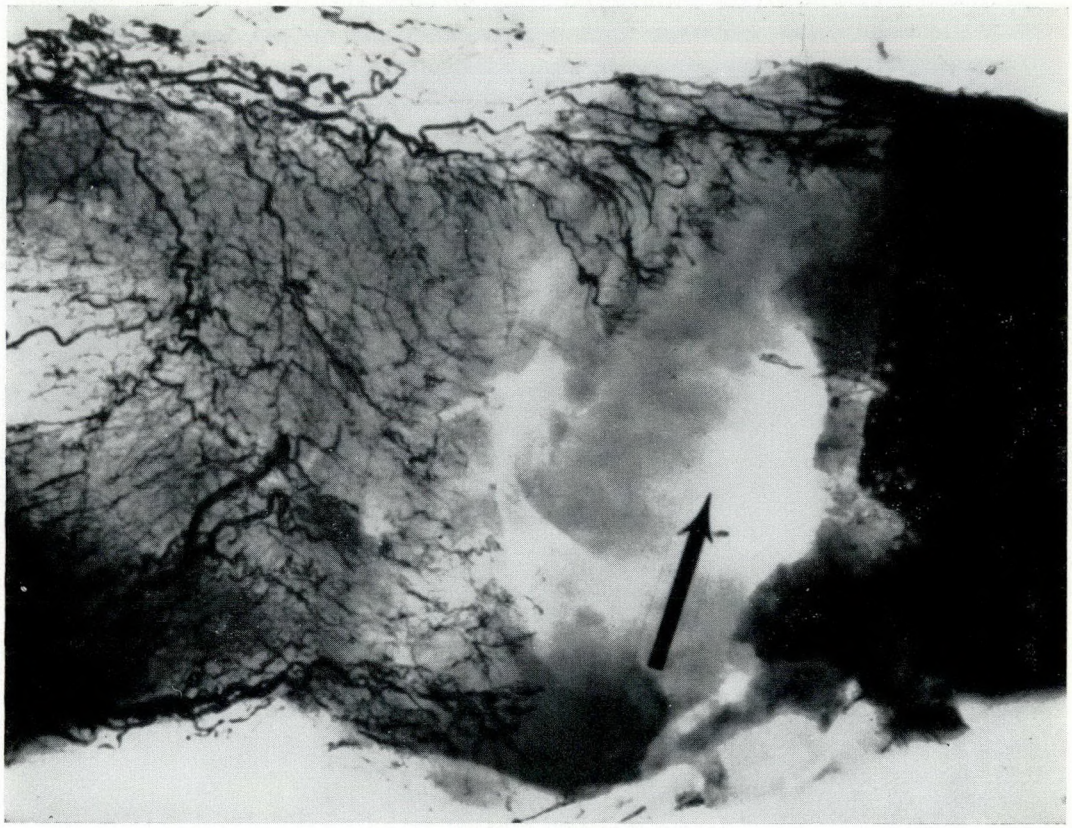

Fig. 3.—Microangiograph of supraspinatus tendon showing area of avascularity.

Elmelik[17] have described a technique to advance the belly of the supraspinatus muscle to allow excision of the degenerated portion of the tendon and implantation of the healthy stump into the tuberosity of the humerus. Theoretically at least, this procedure avoids many of the difficulties inherent in repair of a degenerated tendon.

Summary

From this follow-up study of 71 rotator-cuff tears in 69 patients repaired by several surgeons, we can conclude that: Although 80% returned to gainful employment, nearly one-half returned to modified jobs that placed less demand on their shoulders.

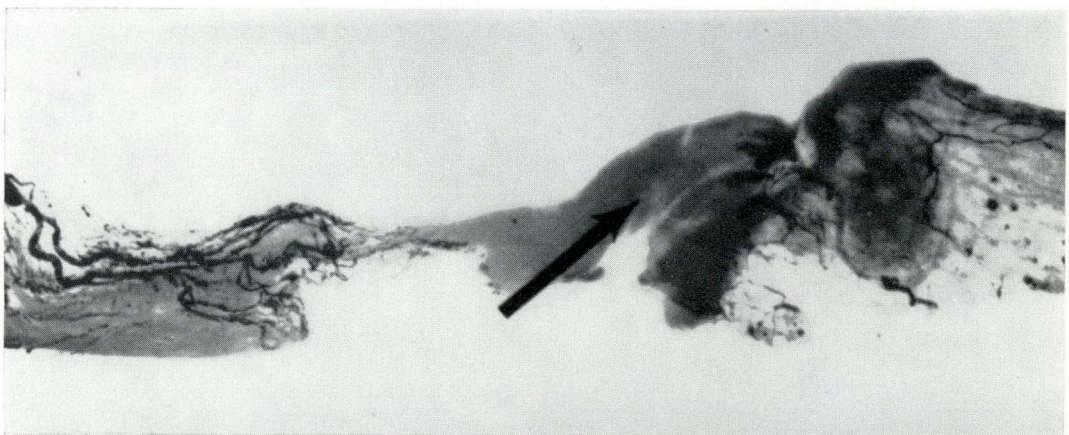

Fig. 4.—Microangiograph of the supraspinatus tendon showing avascular zone and attenuation.

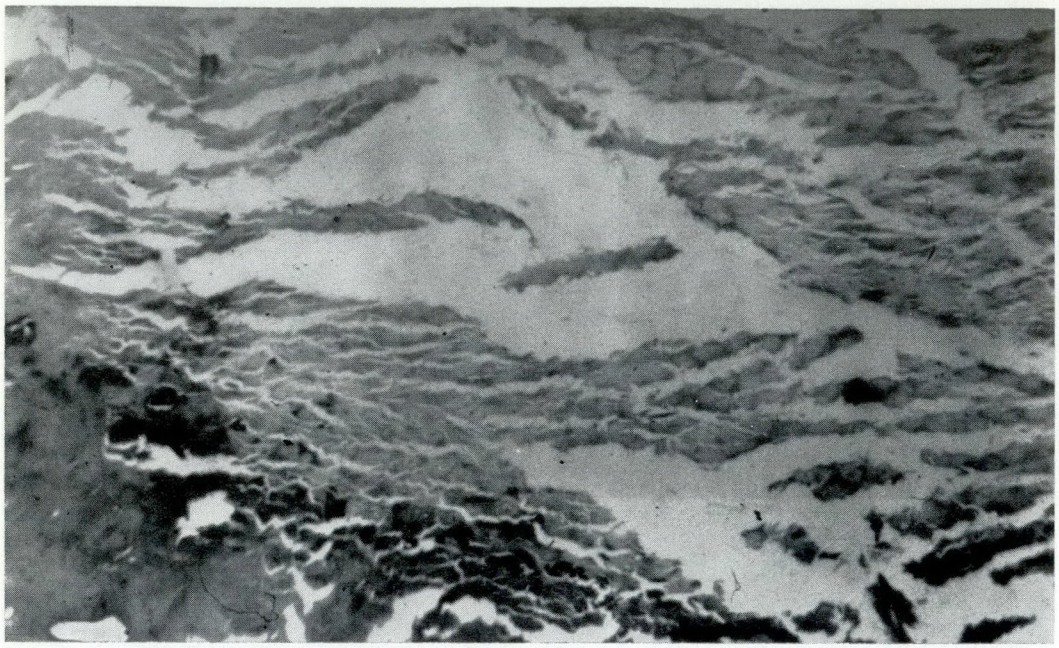

Fig. 5.—Histology of rupture showing fragmented, degenerated tendon fibrils.

The greatest benefit obtained was loss of pain (77%) which may, in part, have been due to spontaneous remission of associated tendinitis. Over one-half (55%) of these patients could not abduct the arm to 90° or could not maintain this position against weak resistance. In this group repair did not give these patients a shoulder that would function normally. Of the patients with unsatisfactory results, most complained of unsatisfactory pain relief and failure to perform at or above the horizontal plane. The underlying pathologic lesion —tendon degeneration—makes it difficult to reconstitute the torn tendon.

The authors are indebted to The Workmen's Compensation Board of Ontario for supporting this study and wish to convey their appreciation to Drs. A. B. C. Powell, H. F. Richardson, and A. W. M. White, to Miss Pat Annesley and staff, Mrs. F. Haas and Mrs. A. Duncan for typing assistance, and to Miss Marlene Bliss and associates for the illustrations.

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Résumé

Les auteurs, après avoir passé en revue 71 cas de déchirure de la coiffe des rotateurs externes opérés par plusieurs chirurgiens chez 69 patients, concluent que, même si 80% de ces malades ont retrouvé un emploi rémunérateur, celui-ci, dans près de la moitié des cas, n'exigeait qu'un effort réduit du malade au niveau de l'épaule. Le principal avantage était la disparition de la douleur (77%) qui peut avoir été causée, du moins partiellement, par une rémission spontanée de la tendinite concomitante.

Plus de la moitié de ces opérés (soit 55%) ne pouvaient procéder à l'abduction du bras à 90° ou ne pouvaient maintenir cette position contre une faible résistance. Parmi les malades de ce groupe, l'opération n'a pu rétablir la fonction du membre.

Chez les malades où l'intervention n'a pas donné de résultats satisfaisants, la majorité se plaignaient de la persistance d'une certaine douleur et de l'impossibilité d'exécuter des mouvements au niveau d'un plan horizontal ou au-dessus de ce plan.

La lésion profonde (soit la dégénérescence tendineuse) rendait difficile la reconstitution du tendon déchiré.

THE NASOPHARYNGEAL ANGIOFIBROMA*

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THE nasopharyngeal angiofibroma, a rare lesion which appears predominantly in adolescent boys, has been described as histologically benign but clinically malignant (Fig. 1). Hippocrates[1] described the bleeding nasal polyp in the fourth century B.C. and, in 1847, Chelius[2] noted that the fibrous nasal polyp was common about the time of puberty. Review of the literature reveals a number of inconsistencies in the tumour's clinical spectrum, its behaviour and its response to treatment. Accordingly, my colleagues and I have studied 31 patients, seen at the Princess Margaret Hospital, Toronto, between 1946 and 1969, in order to draw conclusions about these inconsistencies from this new larger series, 12 of whom were reported in 1967.[3]

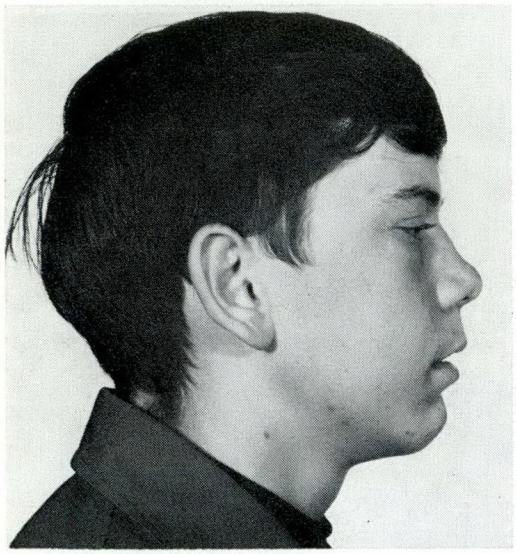

Fig. 1.—Case 12. A 13-year-old boy showing typical features of a juvenile nasopharyngeal angiofibroma, namely, mouth breathing, swelling around the eyes and acne.

MATERIAL AND METHODS

Twenty-eight of these 31 patients were male and three were female (Table I). The median age for males was 14 years 8 months and ranged from 9 to 28 years. The females were 14, 19 and 36 years old. Symptoms, usually present for about one year before diagnosis, included epistaxis, usually severe, nasal obstruction and facial deformity (Table II). We obtained histologic verification of the diagnosis in all, including the female patients. Nine males and two females were evaluated clinically and special studies were done to determine maturation, genetic and endocrine status (seeking evidence of hypogonadism or altered genetic make-up), but all were normal. Clinical underdevelopment in three was not substantiated by laboratory tests; three children were backward at school.

TABLE I.—PATIENTS WITH NASOPHARYNGEAL ANGIOFIBROMA SEEN AT THE PRINCESS MARGARET HOSPITAL BETWEEN 1946 AND 1969

		Age	*Duration of symptoms*
Male	28*	14 yrs. 8 mos. median 9-28 yrs. range	1 yr. median 2 mos.-4 yrs. range
Female	3	14, 19, 36 yrs.	

*Includes one patient treated with radium in 1919 who developed cancer of the nasopharynx 40 years later and one who died at angiography untreated.

TABLE II.—FREQUENCY OF PRESENTING SYMPTOMS IN 31 PATIENTS WITH NASOPHARYNGEAL ANGIOFIBROMA

Symptoms	*No. of patients*
Nasal obstruction—unilateral	21
—bilateral	8
Mouth breathing	1
Nasal voice	2
Nasal discharge	2
Epistaxis	26
Swelling of cheek	6
Proptosis	3
Impaired vision	1
Impaired hearing	2
Headache	3

The incidence of this angiofibroma is unknown but it is probably more common than we realize. Small lesions may be asymptomatic and heal with time, and perhaps only the larger ones come to the physician's attention. The tumour can arise anywhere in the nasopharynx and the symptoms depend on its location. The most common site is the upper lateral nasopharyngeal wall in the region of the posterior choana (Fig. 2). The tumour may be mobile or become adherent to the sur-

*From The Princess Margaret Hospital, 500 Sherbourne Street, Toronto, Ont.

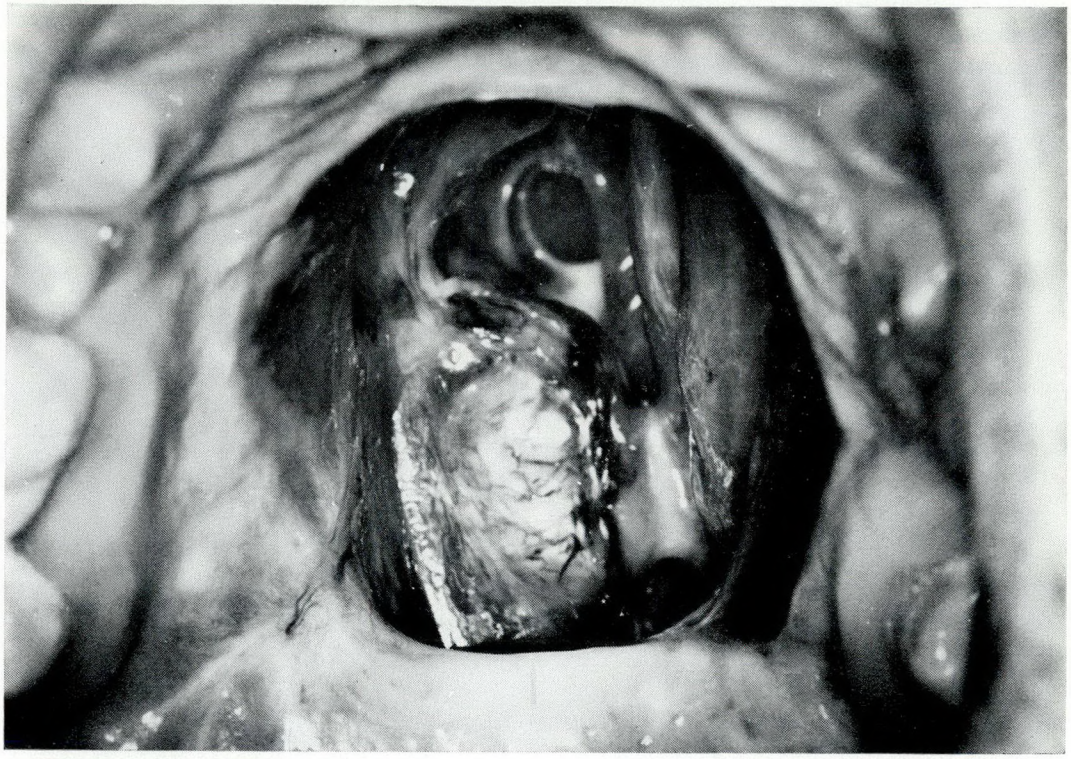

Fig. 2.—Case 12. The palate has been fenestrated and shows the commonest site of tumour on the lateral pharyngeal wall at the posterior choana.

rounding structures obscuring its origin in the nasopharynx: it expands into the space available, particularly the nasal cavity, and may depress the palate. Pressure causes bone erosion. Commonly the tumour may infiltrate the accessory air sinuses and can extend into the orbit and intracranial cavity. The tumour is nodular, bluish red, glistening, frequently ulcerated, and often shows evidence of recent hemorrhage. It obtains its main blood supply from the internal maxillary artery, but ligation of this vessel or the external carotid only partially reduces blood flow to it, showing that it has another blood supply which may come from both the internal or external carotid arteries or from feeder vessels where the tumour becomes adherent to the adjacent mucosa.

In this series the histologic criteria for juvenile angiofibromas were those described by Sternberg in 1954.[4] The tumour consists of angiomatous collagen connective tissue (Fig. 3). Muscle coats of the dilated blood vessels are incomplete and the walls may contain only a single layer of endothelial cells. The connective tissue is loose and both endothelial cells and fibroblasts are immature although tissue matures as the patient grows older. The tumour has no true capsule but compression of the normal mucosa may produce a false capsule.

The etiology is unknown but, because it occurs predominantly in boys, chiefly at puberty, we suspect an endocrine basis. The mucous membrane of the nose has vascular areas of communicating blood spaces similar to erectile tissue, and the sexual apparatus and the nasal erectile tissue appear to have an intimate physiological and pathological relationship.[5] Sexual stimulation may induce nasal congestion, inflammation and bleeding. One physician described a youth who sneezed every time he saw a pretty girl.[6] In many animals, the sense of smell plays a part in sexual stimulation and may account for neurophysiologic connections between the nose and genital system. These angiofibromas, which arise from ectopic foci of nasal erectile tissue in the nasopharynx, respond to hormonal varia-

Fig. 3a

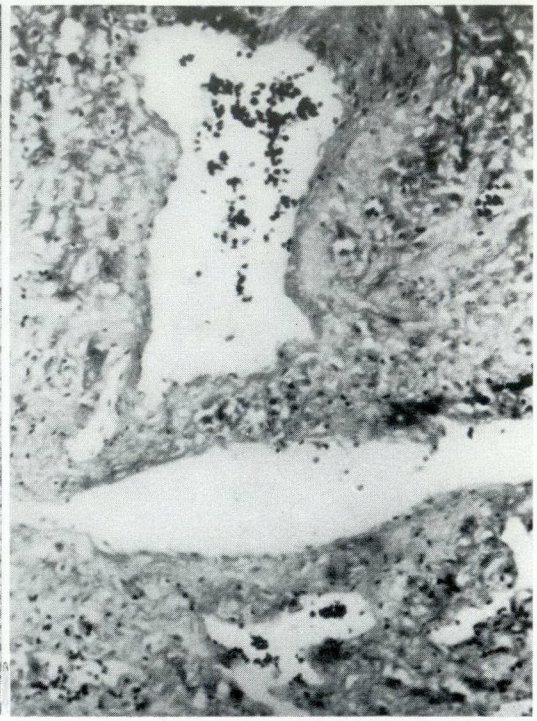

Fig. 3b

Fig. 3.—Nasopharyngeal angiofibroma. (a) Classic appearance of angiomatous connective tissue: note the irregular blood vessels with incomplete muscle coats (H & E, original magnification × 40). (b) Abnormal vessels with incomplete muscle coat or single layer of endothelial cells (H & E, original magnification × 125).

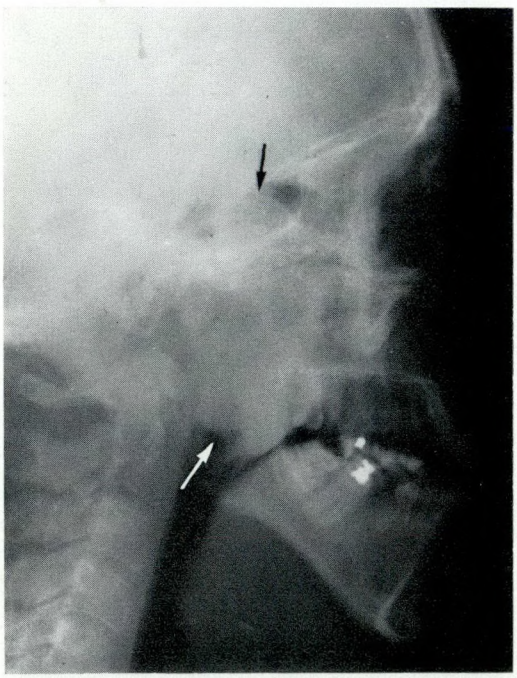

Fig. 4.—Soft-tissue lateral skull radiograph showing large nasopharyngeal mass involving the sphenoidal air sinus.

tions. They are most common in adolescence during the period of growth, and high levels of pituitary gonadotrophins may stimulate their growth.

Clinical Findings and Investigations

The diagnosis can usually be made on clinical grounds, especially when an adolescent boy presents with a mass that causes nasal obstruction, epistaxis and facial deformity. A biopsy should be done in the operating room under anesthesia: facilities for transfusion must be available because severe hemorrhage is common.

Radiographs of the skull may reveal a nasopharyngeal mass (Fig. 4). Coronal polytomography often reveals tumour extensions and bony damage which is unsuspected on clinical examination or the study of routine films, *viz.* Case 14. This 15-year-old boy had a tumour on the lateral wall of the posterior choana and the nasopharyngeal roof recognizable clinically. Routine skull films showed no bony damage but, after serial polytomographs dem-

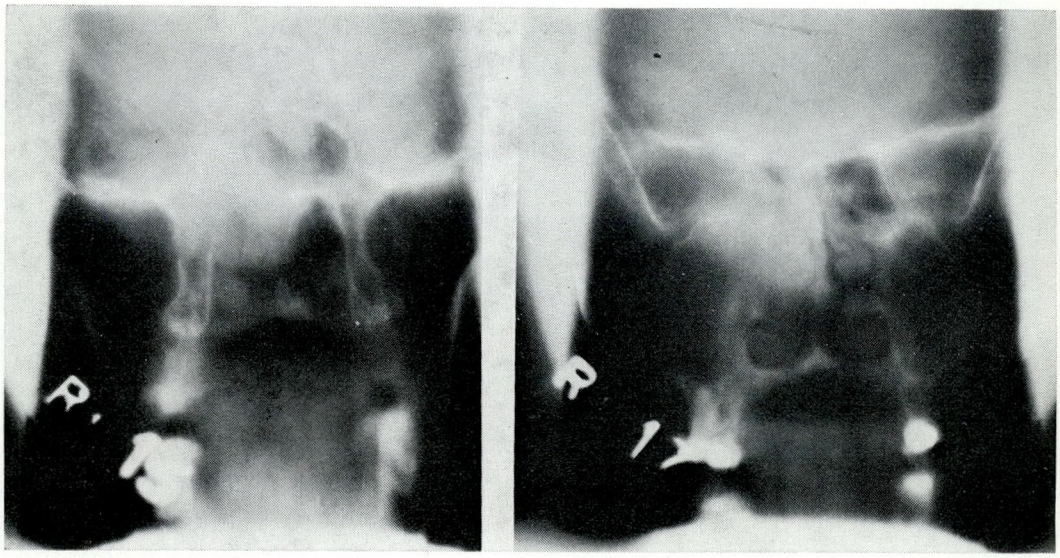

Fig. 5.—Case 14. Serial coronal tomograms of a patient with nasopharyngeal angiofibroma. The erosion of bone and tumour infiltration into the sphenoid and antrum, clearly seen here, were unsuspected on clinical examination.

onstrated erosion and infiltration of the antrum and sphenoid, we were able to irradiate the tumour adequately (Fig. 5). Transaxial tomography is difficult to interpret and with our limited experience we have not been able to evaluate it fully.

Twenty-one of 30 patients had evidence of bone destruction; the sphenoid in 17, the antrum in 14 and the ethmoids in 11, and 14 had more than one bone involved. The orbit was involved in three, and two had intracranial extension which, in one patient, caused almost complete blindness. The frequency of bony erosion is probably

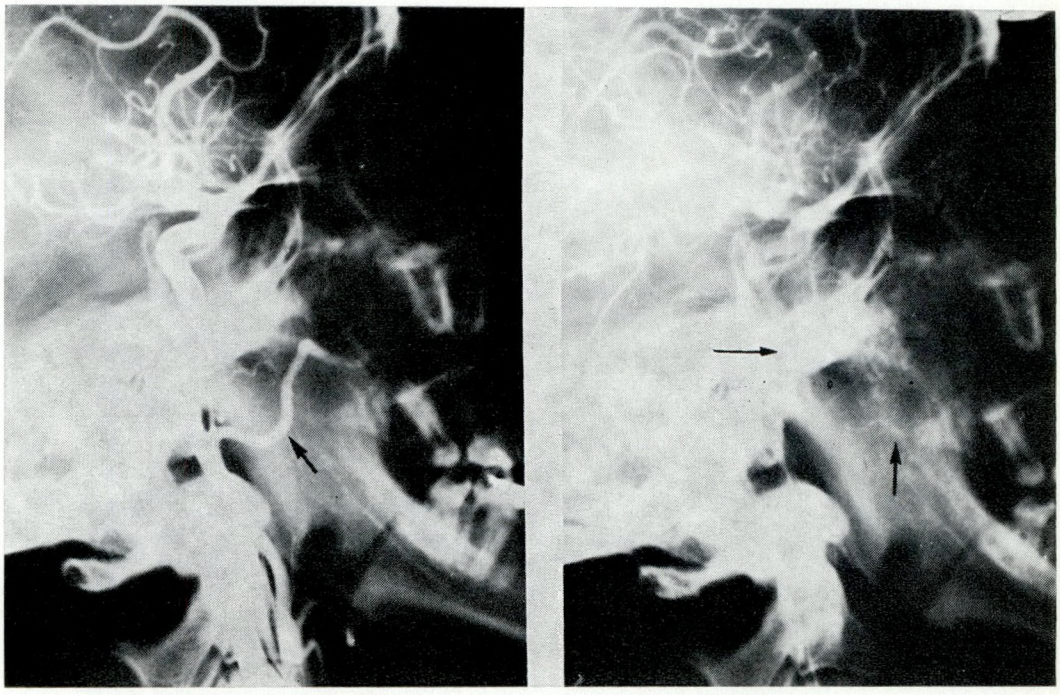

Fig. 6.—Carotid arteriogram showing the enlarged internal maxillary artery and extreme vascularity of the tumour.

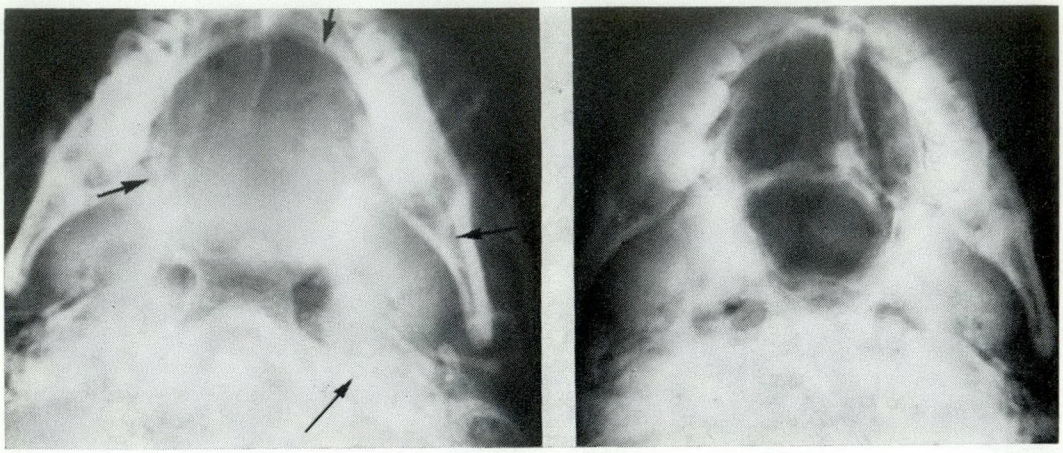

Fig. 7a Fig. 7b

Fig. 7.—Radiograph of the base of the skull showing a large angiofibroma (a) before and (b) six months after ^{60}Co irradiation with a dose of 3000 rads in three weeks.

higher than recorded because the earlier patients in the series were not investigated as completely as those later.

Carotid arteriography, which in recent years has become routine, clearly demonstrates irregular dilated vessels in the tumour, but may not reveal invasion of the air sinuses or cranium. If selective catheterization is done, the blood supply can be localized: bilateral catheterization is probably unnecessary. In 20 patients studied by arteriography, the major blood supply was from the internal maxillary artery, which was often much dilated, but other vessels contributed (Fig. 6). Two tumours received blood from the internal carotid system but in only one patient was a contribution from both right and left carotid systems demonstrated.

Results of Treatment

All patients were treated with irradiation. Because of the good results achieved in our first 12 patients reported in 1967, we recommend irradiation as the first definitive treatment for large nasopharyngeal angiofibromas.[3] Small asymptomatic tumours or those with minimal symptoms can be followed without treatment because they may regress with time, although I know of no documented case in the world's literature. We observed without treating only one patient (Case 24), a 14-year-old boy with a six-month history of nasal obstruction, epistaxis and one surgical resection. In a few months, however, the tumour grew rapidly and we had to irradiate it. Subsequently he had two further resections and a second course of irradiation because of persistent tumour growth and this radiation has just been completed. Another patient (Case 5), after four operations, irradiation, another operation and the administration of androgens, was left with a residual tumour which gradually regressed over several years.

Of the several irradiation techniques available, the choice depends on the extent of the tumour. Vital structures such as the anterior chamber of the eye and spinal cord are fully protected and we have observed no complications, early or late, in these patients. A dose of 3000 rads in three weeks in 15 treatments produces minimal side effects. Symptomatic relief, which begins during treatment, is usually complete several months later. The tumour may regress at once, but up to two years may pass before it finally disappears and occasionally a residual fibrous "nubbin" persists at the site of origin (Fig. 7).

Our experience with these 31 patients is summarized in Table III. Before irradiation, surgical removal, other than biopsy, was attempted 38 times in 16 patients: after irradiation, seven operations were carried out on four patients. Three patients required a second course of irradiation and one patient, who had two operations before irradiation, had three more operations and a second course of irradiation before his

tumour was controlled (Case 12). Fourteen patients had irradiation as the first treatment and only one, Case 14, developed recurrence. Here, radiotherapy failed because we omitted the sphenoidal sinus from the irradiated volume. Ten patients have been followed for more than five years and 17 for more than two years. Seven patients have been followed for less than two years but their clinical pattern appears satisfactory and the initial response to treatment in five is good. Five patients, symptom-free, were lost to follow-up after one year. Only three patients developed a first recurrence more than two years after irradiation and so control at two years is a reasonable index of cure.

TABLE III.—Summary of Treatment of 31 Patients With Nasopharyngeal Angiofibroma

Case no.		*Treatment**	
1		S R	
2		SSS R	
3		R	
4		SSSS R	
5		SSSS R S	Androgens
6		R	
7		R	
8		R	Androgens
9		R	
10	(female)	R	
11	(female)	SS R	
12		SS R SSS R	
13		R	
14		R R	
15		—	Died during angiography
16		SSSS R	
17		S R S	
18		R	
19		SSS R	
20		R	
21		R	
22		R	
23	(female)	S R	
24		S R SS R	
25		SS R	
26		R	
27		R	
28		SSSSS R	40 yrs. later developed cancer of nasopharynx
29		SS R	
30		SS R	
31		S R	

*S = surgery; R = radiation. After irradiation only 5 of 30 patients had recurrences and required further treatment, and of 14 patients receiving irradiation as the first treatment only one had a recurrence.

Discussion

In the recent literature,[7-9] some workers favour operative treatment: improved technique, hypotensive anesthesia and cryosurgery have reduced the blood loss from small tumours, but the large infiltrating lesion is still difficult to remove at operation. Surgical complications are formidable and postoperative deaths have been reported. Some have condemned irradiation because of serious complications including radionecrosis of bone and the late development of squamous cell epitheliomas of the skin and nasopharynx. The patients in this series received minimum doses of 12,000 to 18,000 rads in repeated courses. One patient (Case 28) was treated elsewhere in 1919 when he was 18 by means of radium tubes inserted into the nose and nasopharynx. Over a six-month period, he received a minimum estimated dose of 60,000 rads at 0.5 cm. from the mucosal surface. Before irradiation he had had five resections and the tumour recurred promptly after each, but after irradiation his symptoms disappeared. Unfortunately, 40 years later he developed a squamous cell carcinoma in the nasopharynx and recently this second tumour was irradiated. We believe that repeated radiation is potentially dangerous and that doses greater than 3500 rads should be avoided in benign disease, especially when long survival is expected. A tumour dose of 3000 rads in three weeks is just as likely to produce regression as a higher dosage; if this fails, operation should be recommended. With our radiation technique, morbidity has been negligible and we know of no complications, although some of our earliest patients have been lost to follow-up. On review, when treatment failed it was because we did not recognize that the tumour had extended into the sphenoid, ethmoids or cranium and hence did not adequately irradiate or completely resect the tumour.

Although this tumour occurs chiefly in adolescent boys, similar tumours occur in older males and females. Fig. 8 (Case 23) shows a 14-year-old girl with a classical history of epistaxis, nasal obstruction and swelling of the cheek. The tumour, which histologically was identical with the others, involved both the sphenoid and ethmoidal air cells. After irradiation it regressed rapidly and her symptoms disappeared in two months. Endocrine and genetic studies were normal. Another woman had epistaxis each time she became pregnant. Although we thought three of our male patients had hypogonadism, physical measurements, hormonal assays, including plasma testosterone and urine studies on estrogen excretion, pituitary gonadotrophins, 17-ketosteroids and 17-hydroxycorticosteroids were

Fig. 8.—Case 23. A 14-year-old girl with a nasopharyngeal angiofibroma, which was clinically, radiologically and histologically typical. Many authorities assert that this tumour never occurs in females. Endocrine and chromosome studies were normal.

Fig. 9.—Case 15. Autopsy view of the sphenoidal sinus opened from above to show extensive polypoid tumour ramifications. This is the only untreated autopsy case to be reported.

normal, as were thyroid studies. We treated two males with androgens without improvement and are considering treating another with estrogens. The literature describes six patients in whom the tumours shrank and became less vascular with stilbestrol therapy; this is now recommended as a preoperative treatment.[7, 10] However, estrogen, particularly in adolescent males, may limit growth by stimulating the maturation of the bony epiphyses. Androgens may stimulate the development of the angiofibroma although there are reports that this hormone brings the growth of the tumour to a standstill and decreases the bleeding tendency.[11] Johnsen, Kloster and Schiff[10] report that angiofibromas enlarge on androgen therapy and subsequently shrink on estrogens. The hormonal status and treatment of these tumours is confusing and further studies are required.

The only death in our series was a tragedy due to idiosyncrasy either to the contrast agent or anesthetic used for angiography. This 16-year-old boy is the only untreated case to come to autopsy and be reported. About 40 minutes after the procedure began, the boy developed a high temperature with tachycardia and hypotension, became comatose and neurologically inert. He began to bleed from the nose and throat and into the skin, became acidotic and oliguric, and died 10 hours later from cerebral edema. He had complained of right-sided nasal obstruction and severe epistaxis for three months. On clinical examination he was normal and had a large tumour mainly on the right side of the nasopharynx. Eighteen days previously a biopsy, which had confirmed the diagnosis, had been obtained under anesthesia without complication. Routine skull films showed the mass, and lateral tomograms showed that it was about 4 cm. in diameter, arose from the roof of the nasopharynx and infiltrated the sphenoidal sinus. A right carotid arteriogram confirmed that it was vascular and infiltrated the sphenoidal sinus. At autopsy we found an enormous, red, lobulated, vascular tumour, 6 cm. at its greatest diameter, which arose from the roof of the nasopharynx, destroyed the anterior sphenoidal wall and filled the sinus (Fig. 9). Because the tumour was so much larger than we had anticipated and because other patients may have had similar extensions, we have made tomography and angiography routine since this experience.

In retrospect, our good results reported previously[3] may have been due to an element of luck because earlier patients were not exhaustively investigated and most were treated with small opposed fields covering the roof of the nasopharynx, but sometimes omitting the sphenoidal sinus. Recurrence would appear to be due to failure to destroy or remove the tumour completely because widespread ramifications do penetrate the surrounding sinuses, orbit or cranium.

Summary

Thirty-one patients, including three females, with nasopharyngeal angiofibromas were seen at the Princess Margaret Hospital, Toronto, between 1946 and 1969. Twenty-one of 30 patients had bone destruction and involvement of the accessory air sinuses. Because residual tumour in these areas appears to lead to recurrence, tomography must be done to reveal unsuspected extensions. Two patients had intracranial extension and three had involvement of the orbit. One patient died during arteriography and, at autopsy, this tumour proved to be more extensive than anticipated. One patient treated 40 years ago with radium at a minimum dose of 60,000 rads developed a carcinoma of the nasopharynx. Three thousand rads in three weeks leads to thrombosis, fibrosis and tumour regression, although up to two years may pass before it finally disappears. Of 14 patients irradiated as the first planned treatment, only one developed a recurrence and after irradiation only 5 of 22 patients at risk for two years or more required further treatment.

These patients were investigated and treated by various members of the radiotherapy staff of the Princess Margaret Hospital and I am grateful to them for allowing me to describe their patients. In particular, Dr. W. D. Rider generated the philosophy of management and advised and encouraged me to report this material. Many surgeons referred these patients and without their co-operation and help this series could not have been assembled and this experience reported. Dr. W. Meakin advised on the endocrine assessment of patients and Dr. T. C. Brown reviewed the microscopic slides and confirmed the diagnosis of angiofibroma. My sincere thanks go to the Department of Medical Photography for the preparation of the figures and tables, and to my secretary, Miss Doris Hunter, for typing the manuscript.

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Résumé

A l'Hôpital Princesse Margaret de Toronto, nous avons eu l'occasion de voir, de 1946 à 1969, 31 malades, dont trois femmes, souffrant d'angiofibrome nasopharyngien. Chez 21 des 30 malades, on notait de la destruction osseuse et une atteinte des sinus accessoires. La tumeur résiduelle dans ces régions ayant tendance à récidiver, il importe de procéder à une tomographie pour déceler une extension inattendue. Chez deux malades, cell-ci s'est produite à l'intérieur du crâne et chez un autre, au niveau de l'orbite. Un patient est décédé pendant l'artériographie: à l'autopsie, on constata une propagation tumorale plus étendue qu'on ne le croyait. Chez un malade traité par radiumthérapie 40 ans auparavant à une dose minimum de 60,000 rads, se développa un cancer du nasopharynx. L'application de 3000 rads en trois semaines a provoqué de la thrombose, de la fibrose et la régression de la tumeur, mais il ne faut pas oublier qu'il faut compter deux ans avant qu'elle ne disparaisse complètement. Des 14 malades traités par irradiation comme premier traitement, un seul subit une récidive et, après irradiation, cinq seulement des 22 malades ont dû recevoir un nouveau traitement.

INVESTIGATION OF AUTOMOTIVE MISHAPS IN FRONTENAC COUNTY (ONTARIO)*

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In the 12 months of 1966, 5258 Canadians were killed on our highways and 160,656 injured. Fifteen to 20% of the injured have not, and will not, return to the "normal" life they left at the moment of accident impact. Thus, in one year 34,176 Canadians were removed from effective participation in the affairs of the community. The approximate cost of this one year's traffic accidents is shown in Table I.

TABLE I.—Traffic Accident Costs for 1966 in Canada (in Millions of Dollars)

Property damage	460
Hospital costs	36
Medical costs	40
Legal fees	50
Loss of time benefits	100
Loss of gross national product	320
Total	$1000*

*Figures estimated from statistical breakdown of accident costs for City of Washington, D.C., 1966. A yearly increase of 15% is predicted.

The investigation of an epidemic requires thorough appraisal of all variables including agent, host, and environment. In the current epidemic of traffic deaths, an investigator must study automotive accidents with simultaneous and complete reference to the vehicle, the driver and the environment. The interaction of these three variables presents a multitude of permutations and combinations of facts and events. In earlier studies we identified about 1500 items or facts that may be significant in the investigation and assessment of a traffic accident. These 1500 items, which have been reduced to a "check list" form of input for computer storage and analysis, form the basis of our investigation manual.[1] The investigation manual is divided into five sections under the headings: General Instructions and Notes, Accident Identification, Environment Data; Driver Data; Occupant Information, Tissue Damage; Vehicle Information; and Key Words—Location Codes. This manual has 39 pages and Fig. 1 shows one of its pages.

In the final analysis, all accidents are due to a failure of the driver, the vehicle, or the environment. In this regard failure of the driver to react swiftly and surely to prevent an accident is easily understood. Failure of the vehicle, particularly tires, brakes, or steering, may also produce an accident. Failure of the environment is more difficult to understand and an example may be helpful. In one accident we investigated, two cars were approaching a bridge marked by signs reading "Narrow Bridge". In reality the bridge was only one lane and, consequently, one driver was forced into the bridge railing when he found there was not enough room for two cars. He survived the injury, and two days later the road signs were changed to read "Danger One Lane Bridge".

A review of the literature on the subject of highway accident investigation disclosed Mosley's report from Harvard[2] in 1962. In this study, in a five-year period, 114 fatal accidents were investigated in depth; this included a complete review of the driver, the vehicle, and the environment. The study employed 15 persons and the total cost was approximately $810,000—a small amount considering that the investigation of 124 deaths in the Air Canada crash near Montreal in 1964 cost $5,500,000.

At Queen's University, Kingston, we in the Automotive Crash Research Unit (A.C.R.U.) believed we could reduce the costs in personnel and money and in the process develop effective data collection methods. To this end, the A.C.R.U. was formed in 1966, drawing on personnel from medicine, engineering, psychology, law, computer sciences and biostatistics.

A pilot project, begun in 1967 and completed in 1968, developed an efficient

*From the Automotive Crash Research Unit (A.C.R.U.), and the Department of Surgery, Queen's University, Kingston, Ont.

Representative page from A.C.R.U. Investigation Manual.

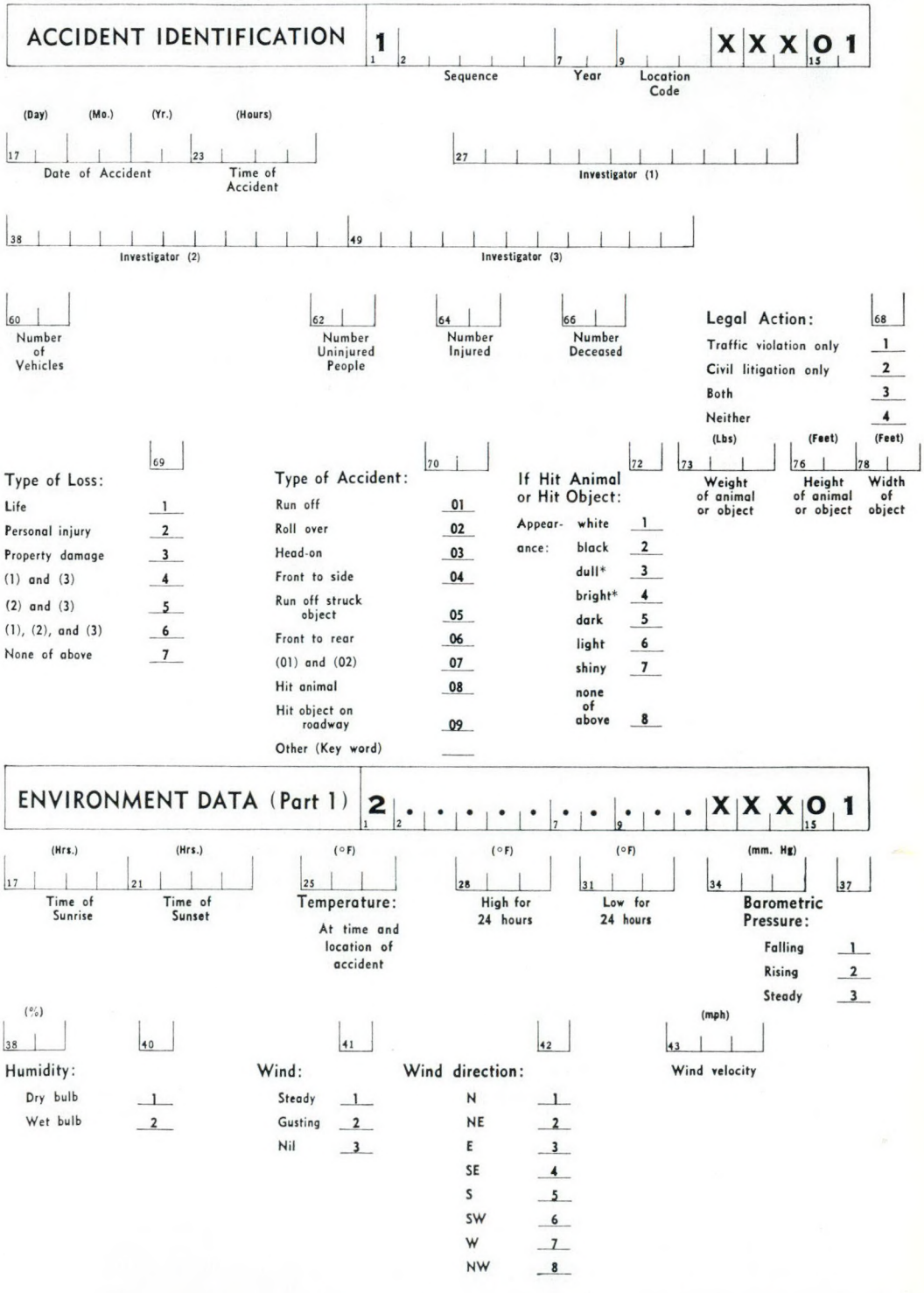

Fig. 1.—Representative page from the A.C.R.U. investigation manual.

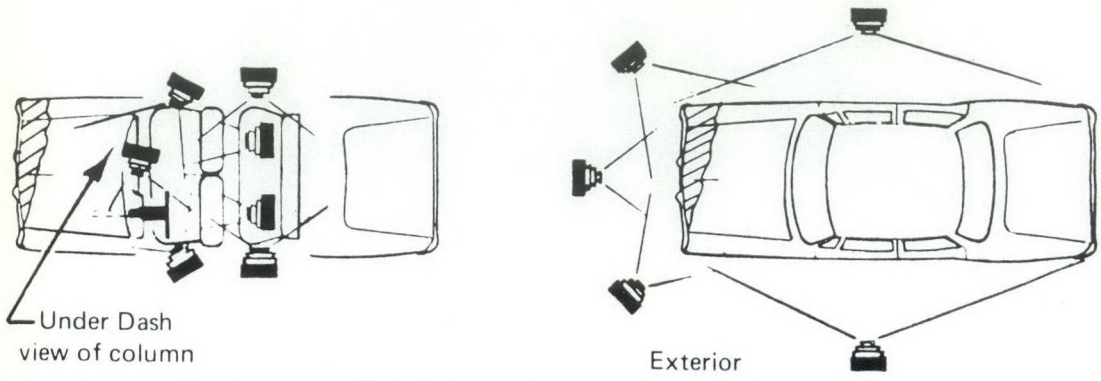

Fig. 2.—Vehicle photo requirements (front-end wreck shown).

means of accident data collection and a method to store and analyze this data. The reports in the literature to that date had been superficial, and few had simultaneously evaluated all of the variables concerned in a traffic accident.[2]

Material and Methods

The study reported in this paper was done between June 15 and September 3, 1967, and during the same period in 1968. The research crew was picked from undergraduates in medicine, engineering, and law, and they were trained by the senior author in a three-week period before the study began. This training was supplemented by a review of the accident investigation literature.[3-6] The crew worked from a Ford Econoline van equipped with a two-way radio which was in contact with a telephone answering service. In addition, each member of the crew carried a pocket "Pagemaster", a small unit through which he could be contacted at all times.

The Kingston City Police Department, or the Ontario Provincial Police, Kingston Detachment, notified the research crew of all serious accidents. This co-operation enabled the crew to arrive at the accident shortly after the police and ambulance vehicles.

When notified of a serious accident, at least two members of the research crew were dispatched to the scene: one became the prime investigator for that specific accident. On arrival at the scene, he recorded all possible data about the scene (environment) and the vehicle. The second investigator took standard photographs (35 mm. colour slides) of the vehicle itself (Fig. 2), and of the roadway and other parts of the environment that may have contributed to the accident. The second (and third investigator if present) then assisted the prime investigator in measuring all skid marks, ditch depths, shoulder widths, temperatures, wind velocity and so on. These facts were recorded in the investigation manual. Witnesses were interviewed at the scene and survivors of the accident at the scene or later in the hospital emergency area.

The driver received special attention in follow-up interviews and all pertinent details of his past life were recorded if he survived and was able to give information. Relatives, friends or acquaintances were interviewed if the driver had been killed. Thus we produced a profile of medical health, financial status, job status, marital status, etc.

The Chief Coroner ordered autopsies on all deceased drivers and, from this information, we were able to correlate injuries and points of impact on the vehicle's interior or the environment if the driver was ejected (second collision). This part of the study will be reported in a separate communication.

If anyone had been killed in the accident, the Coroner impounded the vehicle. If not, we obtained signed permission from the owner, and the vehicles were examined carefully by a qualified Class A mechanic. These automotive "autopsies" were recorded in the check list investigation man-

ual. All vital areas of the vehicle were photographed during the examination. If the investigators detected material failure, metal or rubber components were sent to the laboratory for detailed analysis.

Observations

In the six summer months of 1967 and 1968, the research crew studied 31 accidents at a total cost of $12,500. The present report describes the findings in 16 fatal accidents and 15 non-fatal accidents (Table II). These 31 accidents involved 140 people; 23 were killed, and 88 injured. The cause of death determined at autopsy confirms that, in these 23 patients as in previous series, head injuries lead the list (Table III).

TABLE II.—Figures From 31 Accident Investigations

	Bicycles	*Motor-cycles*	*Camper trailer*	*Bus**	*Car*	*Total*
No. of vehicles	1	2	2	1	38	44
Drivers:						
Dead	1	2	—	—	10	13
Injured	—	—	—	1	19	20
Uninjured	—	—	—	—	9	9
Total						42
Passengers:						
Dead	—	1	—	1	7	9
Injured	—	—	—	37	29	66
Uninjured	—	—	—	—	21	21
Total						96
Pedestrian:						
Killed†	—	—	—	—	1	1
Injured	—	—	—	—	1	1
Total						2

*Intercity bus accident accounted for 38 injuries and one death.
†Child pedestrian killed by run-off (car) on her own front lawn.

Single Vehicle Accidents

Single vehicle accidents accounted for 9 of 16 fatal accidents. The run-off/roll-over type was most common and occurred six times. In the non-fatal accidents, 10 of 15 were single vehicle accidents and, of these, three were "run-off/roll-overs" (Table IV).

TABLE III.—Causes of Death

Cause	*A.C.R.U. series*
Craniocerebral injuries	11/23
Chest injuries	6/23
Burns*	4/23
Abdominal injuries	1/23
Musculoskeletal injuries	1/23

*This series contains a high incidence of burn fatalities because four people died of burns in one accident in which a car caught fire.

TABLE IV.—Single Vehicle Accidents

Type of accident	*Fatal*	*Non-fatal*	*Total*
Single vehicle	9	10	19
Run-off/roll-over	6	3	9
Run-off	—	3	3
Run-off/struck object	2	3	5
Car-pedestrian	1	1	2
Ejection	3	3	6

In spite of advertising claims, cars in the 1960's that had a low centre of gravity had a depressing tendency to roll. Such cars with drivers and passengers unrestrained by seat belts set the stage for danger and death. Only 4 of the 140 people in this investigation were wearing seat belts at the time of impact. These four were not injured. Four of the nine people killed in single vehicle accidents would have survived had they been wearing seat-belt restraints. Three of these deaths were due to ejection.

Faulty design—soft or hard-top convertibles with no roll bars—contributed to four deaths in the single vehicle group. In roll-over situations these roof structures did not give adequate protection.

TABLE V.—Multiple Vehicle Accidents

Type of accident	*Fatal*	*Non-fatal*	*Total*
Two vehicle	7	5	12
Side penetration	3	2	5
Head-on	2	1	3
Car-bicycle	1	0	1
Car-motorcycle	1	0	1
Car-trailer run-off	0	2	2
Ejection	0	3	3

Multiple Vehicle Accidents

Seven of 16 fatal accidents, and 5 of 15 non-fatal accidents were two vehicle accidents (Table V). Five of these were front-to-side "smashes" in which the side of the struck vehicle was penetrated from 5 to 22 inches.

In two head-on crashes, four persons died from chest or cardiac injuries; these and the ejection deaths would have been prevented by lap-diagonal type restraints. Thus, in this series, an adequate passenger restraint at the time of impact would have reduced the death toll in Frontenac County by 35% (8/23).

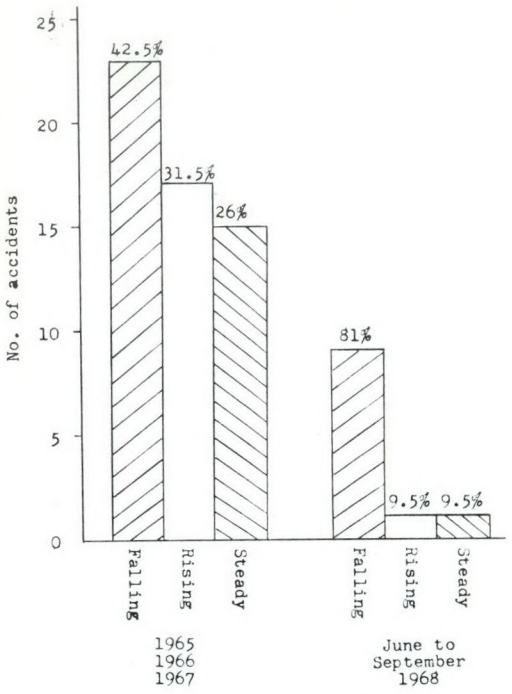

Fig. 3.—Barometric pressure related to fatal accidents in Frontenac County.

Barometric Pressure and Accident Rate

One curious fact concerning barometric pressure became evident during our investigations. In 81% of fatal accidents and 73% of non-fatal accidents, the barometric pressure was falling at the time of the accident. This prompted us to review barometric pressure in relation to automotive mishaps in our area for the past three years. In 1965, 1966 and 1967 the number of serious automotive mishaps tended to increase during periods of falling atmospheric pressure (Fig. 3). Some workers in this field have suggested that this correlation is due to a change in ionization of inhaled gases, particularly oxygen and nitrogen.[7]

Dirnagl[8] in 1967 reported that industrial accidents in Switzerland increased 20% during periods of low barometric pressure coincident with the Föhn wind. Hippocrates also expressed an interest in biometeorology when he stated: "Whoever wishes to pursue properly the science of medicine must proceed thus. First he ought to consider what effects each season of the year can produce: for the seasons are not alike, but differ widely both in themselves and at their changes."[9] We are now investigating the "physical/mental performance index" of animals under varying barometric pressures and will report the results of this study later.

Causality Assessment

At the completion of an investigation, we assigned to each accident an initiating cause and a reinforcing cause. This subjective evaluation is open to criticism but until we have a mathematical model of an accident situation, this weakness will remain. The term "initiating cause" refers to the failure of the driver, vehicle, or environment that started the train of events that ended in the automotive mishap. "Reinforcing cause" applies to any factor in the driver's reaction, the vehicle's response, or the environmental surroundings that "reinforced" an initiating event and produced an accident. We have observed that each accident has a "point of no return", and if corrective action is prevented or delayed by any factor in the driver, vehicle, or environment, a mishap follows. Thus, we consider that the driver, vehicle, or environment has "failed".

TABLE VI.—Causality Assessment—Driver Failure

Initiating cause				*Reinforcing cause*		
Fatal	*Non-fatal*	*Total*		*Fatal*	*Non-fatal*	*Total*
			Driver failure			
7	6	13	Alcohol	—	—	—
3	—	3	Speed	2	1	3
2	—	2	Inexperience	4	2	6
1	3	4	Inattention	—	2	2
1	—	1	Illness	—	—	—
—	—	—	Age	1	—	1
14	9	23	Total	7	5	12

Driver Failure (Table VI)

Twenty-three out of 31 accidents—14 fatal and nine non-fatal—were classed as driver failure. Thirteen drivers had consumed alcohol to an extent that made it a factor. In one non-fatal accident, a driver lost control of his vehicle while reaching for another can of beer from the cockpit floor. In this one case at least, we have definite proof that alcohol can cause an accident. Speed was the initiating cause on three occasions. Driver inexperience and inattention to the driving act were responsible for six accidents.

TABLE VII.—Causality Assessment—Vehicle Failure

Initiating cause				*Reinforcing cause*		
Fatal	*Non-fatal*	*Total*		*Fatal*	*Non-fatal*	*Total*
			Vehicle failure			
—	—	—	Maintenance	2	1	3
—	1	1	Steering	1	—	1
—	—	—	Brakes	—	2	2
1	1	2	Tires	—	1	1
—	—	—	Shock absorbers	—	1	1
1	2	3	Design	—	1	1
—	1	1	No seat belts	6	1	7
—	—	—	No roll bar	3	—	3
—	—	—	No helmet (motorcycle)	1	—	1
2	5	7	Total	13	7	20

In our series, reinforcing causes were multiple; in 12, such reinforcement contributed to driver failure in the form of speed (three times), inexperience (six times), inattention (twice) and age (once).

Vehicle Failure (Table VII)

Factors in vehicle maintenance or design initiated the accident on seven occasions: faulty steering (once), poor maintenance of tires or tire pressure (twice), and faulty design (three times). In two accidents, camper trailers were inadequately balanced or inadequately "hitched" to the automobile.

Twenty causes of reinforcement were blamed on the vehicle: poor maintenance (three times), no seat belts (seven times) and inadequate roof support (three times). Arbitrarily, we blamed the vehicle for not insisting that seat belts be used—a patent misdirection of blame.

Environmental Failure (Table VIII)

In our series, we found that in most instances the environment in which we drive was safe; it initiated only one accident. However, environment, namely poor highway maintenance and poor shoulder design reinforced 13 accidents. A "drop-off" from paved roadway to gravel shoulder of three to four inches was a major factor in three fatal accidents, when combined with the driver's inexperience in the proper method of regaining the paved roadway.

TABLE VIII.—Causality Assessment—Environmental Failure

Initiating cause				*Reinforcing cause*		
Fatal	*Non-fatal*	*Total*		*Fatal*	*Non-fatal*	*Total*
			Environmental failure			
—	—	—	Road design	—	1	1
—	—	—	Shoulder design	3	2	5
—	1	1	Highway signing	1	1	2
—	—	—	Guard rails	2	1	3
—	—	—	Road maintenance	1	1	2
	1	1	Total	7	6	13

TABLE IX.—Type of Roadway and Accident Frequency

Type of roadway	*Fatal*	*Non-fatal*
Freeway	3	1
Arterial	4	4
Collector	5	8
Local	4	2
Total	16	15

The relationship between the type of roadway and accident incidence is of some interest (Table IX). Only four of our accidents occurred on freeways; in three of these someone was killed and of these three, two were roadway/shoulder "drop-offs". Thirteen accidents took place on county or township roads. These roads were constructed some time ago, and could not now meet present minimum standards. Thus, poor highway construction must be considered in our causality assessment.

It is commonly thought that more serious accidents occur after dark. Our investigation showed the opposite: only 12 of the 31 accidents occurred during the night.

Driver Age

In our series, young drivers were involved in a greater number of serious accidents: 9 of 16 fatal accidents involved drivers under age 25. Six of 15 non-fatal accidents involved the same age group. However, until we can compare such figures with the number of miles driven by all age groups we can draw no conclusions.

Summary

Conclusions cannot and should not be based on a small series such as ours. However, some preliminary observations might be in order.

An effective method of data collection for motor vehicle accidents has been developed and tested.

A larger series of in-depth accident investigations on a continuing year-round basis is needed before remedial measures can be suggested, be they legislative, edu-

cative, corrective, or punitive. Facts not fancy must be obtained before the mounting traffic toll can be contained.

Alcohol made a considerable contribution to driver failure in our series of accidents. It was a factor in 58% of mishaps classed as driver failure.

In our series, few people involved in accidents wore seat belts. If lap-diagonal belts had been worn, 35% of the deaths could have been prevented.

At the present time, the use of seat belts offers the simplest and quickest means of reducing the death and injury toll from motor vehicle accidents.

The authors wish to acknowledge the co-operation of the following: The Traffic Injury Research Foundation of Canada; the Faculty of Medicine, Queen's University, Kingston, Ont.; Ford Motor Company of Canada Limited, for the supply of the research vehicles; Ontario Provincial Police, and the Kingston City Police Department; Crown Attorney's Office, County of Frontenac; Coroner's Office, County of Frontenac; and Doug's Emergency Services (Kingston), J. L. Edwards Limited (Ford Dealer), and Carl's Place, G.M. Dealer, Gananoque, Ont., for the provision of Class A mechanics.

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Résumé

Nous avons mis au point et mis à l'épreuve une méthode efficace de recueillir des renseignements sur les accidents d'automobile. Avant de pouvoir préconiser des remèdes à ces situations, qu'ils soient d'ordre législatif, éducatif, correctif ou punitif, il faudra pouvoir disposer de statistiques considérables sur les enquêtes des accidents, tout au long de l'année. Avant de pouvoir enrayer la montée croissante du tragique bilan de la route, il faudra obtenir des renseignements précis et sérieux.

Dans la série d'accidents que nous avons analysés, l'alcool jouait un rôle important. Dans 58% des accidents attribuables au conducteur, l'alcool était un facteur important.

Dans notre série, on trouve peu de conducteurs qui portaient des ceintures de sécurité. Si la ceinture à la taille ou la ceinture diagonale avait été portée, on aurait pu prévenir 38% des décès.

A l'heure actuelle, les ceintures de sécurité sont encore le moyen le plus simple et le plus sûr de réduire les décès et les blessures dans les accidents d'auto.

STRESS ULCER

The first sign of stress ulcer is usually massive bleeding from or perforation of the stomach. This occurs most frequently after an operation, and is often lethal. The authors developed an experimental model in guinea pigs by giving doses of histamine in beeswax that alone would not produce ulceration; when these combined with hydrocortisone they caused perforation regularly. This model was used in conjunction with a study of 83 patients with stress ulcers to delineate the characteristics of the lesion.

In man, the peak incidence of stress ulceration occurred on the fourth and fifth days after operation and in guinea pigs on the fourth day of the combined medication. In the hypersecreting animal and in the patient, infection was associated with multiple gastric ulcers. Gastric resection salvaged 48% of the patients whereas medical treatment saved only 27%.

A physiologic approach to the gastric hypersecretion and decreased mucosal resistance of stress ulceration requires resection, with or without vagotomy.—Douglass, H. O. and LeVeen, H. H.: Stress ulcer: clinical and experimental study showing roles of mucosal susceptibility and hypersecretion, *Arch. Surg. (Chicago)*, **100:** 178, 1970.

BRONCHIAL ARTERIAL CIRCULATION RESTORED AFTER REIMPLANTATION OF CANINE LUNG

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ONLY the bronchial arterial circulation carries arterialized blood at systemic pressures to the normal lung. This circulation must be divided at the time of lung transplantation, and previous studies[1-4] attempted to evaluate the functional alterations in the lung due to this interruption of the bronchial circulation. Most of these investigators concluded that this interruption does not produce significant functional abnormalities after transplantation. However, none of these studies examined the fate of the bronchial circulation after its interruption.

Previous observations from our laboratory[5] indicate that dogs re-establish a vigorous bronchial arterial flow within four weeks of bronchial artery division. Furthermore, we noted that when bronchial circulation was restored, some parameters of pulmonary function returned to normal. Blank, Lower and Adams[6] demonstrated that in the dog the bronchial arterial network regenerated spontaneously some time during the year following left lung autotransplantation.

The present paper reviews in more detail the observations briefly recorded in our previous report[5] and describes observations from a further study of the bronchial arterial circulation following reimplantation of the canine lung.

PART I: BRONCHIAL ARTERY REGENERATION AFTER RADICAL HILAR STRIPPING

In this investigation an experimental model was designed which completely interrupts the bronchial artery circulation and simulates lung reimplantation, but eliminates the complications of reimplantation other than those arising from division of the bronchial arteries, nerves and lymphatics.

Method

In 20 dogs, using pentobarbital sodium anesthesia, the hilum of the right lung was dissected and stripped, leaving intact only the bare pulmonary artery and veins. This required wide anterior incision of the pericardium. The bronchus was divided just proximal to the upper lobe orifice and reanastomosed with a continuous 4-0 silk suture. Before operation selective right bronchial arteriography was done on all dogs using the Seldinger technique. After operation these animals were followed with interval bronchoscopy, repeat selective bronchial arteriography, pulmonary function studies and, at the time of sacrifice, latex injection of the bronchial arterial tree. Pulmonary function was assessed by recording the differential oxygen uptake and minute ventilation using bronchospirometry, and pulmonary artery pressure.

Results

Observations at bronchoscopy.—All animals underwent bronchoscopy at intervals from one day to eight weeks after operation. At bronchoscopy all dogs had some evidence of impaired circulation to the bronchial mucosa distal to the line of anastomosis (Fig. 1). The mucosal changes were characterized by edema, cyanosis and retention of secretions distal to the level of division of the bronchus. In 17 of the 20 animals these changes gradually resolved and disappeared within six weeks of operation (Fig. 2).

One dog developed severe bronchial stenosis at the suture line within six weeks of operation. Two dogs developed bronchopleural fistulas within two weeks of operation, and at the time of sacrifice

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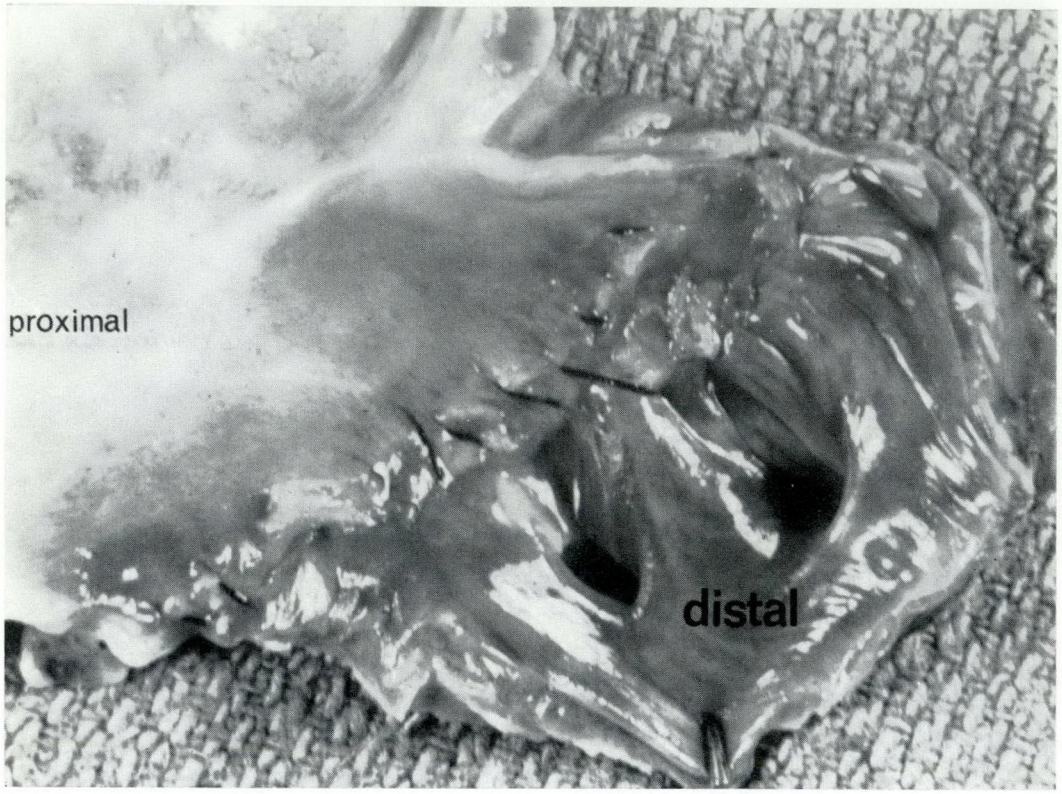

Fig. 1.—Mucosal aspect of the bronchial anastomosis in a dog killed five days after radical hilar stripping and division of the bronchus. On the distal side of the suture line the mucosa is edematous, congested and cyanosed, reflecting impaired bronchial arterial circulation.

had small areas of ischemic necrosis in the bronchial wall on the distal side of the anastomosis.

Selective bronchial arteriography.—Before operation a satisfactory selective bronchial arteriogram was obtained in 15 of the 20 dogs. The distribution of the bronchial arterial circulation in the dog is shown in Fig. 3 and a normal, preoperative bronchial arteriogram in Fig. 4.

Postoperatively repeat selective bronchial arteriography was attempted in nine dogs, and a successful arteriogram was obtained in seven, from six weeks to five months after operation. All seven had re-established a vigorous bronchial arterial circulation which appeared comparable to that demonstrated in the preoperative arteriogram. Fig. 5 shows the appearance of the postoperative arteriogram at 43 days.

Latex injection of the bronchial arteries.—In 12 dogs killed from one week to five months after operation, we injected the origin of the right bronchial artery with coloured latex at thoracotomy, immediately before sacrifice. The eight animals sacrificed after four weeks or more had a grossly normal bronchial arterial circulation (Fig. 6). The four dogs sacrificed earlier than four weeks had no demonstrable restoration of circulation.

Part II: Bronchial Artery Regeneration After Reimplantation of the Lung

This part of the study was designed to assess alterations in the bronchial arterial circulation after autotransplantation of the canine lung.

Method

Autotransplantation of the lung was done in 15 dogs under nitrous oxide and Penthrane anesthesia. We mobilized the lung by wide circumhilar incision of the pericardium, and divided the pulmonary ar-

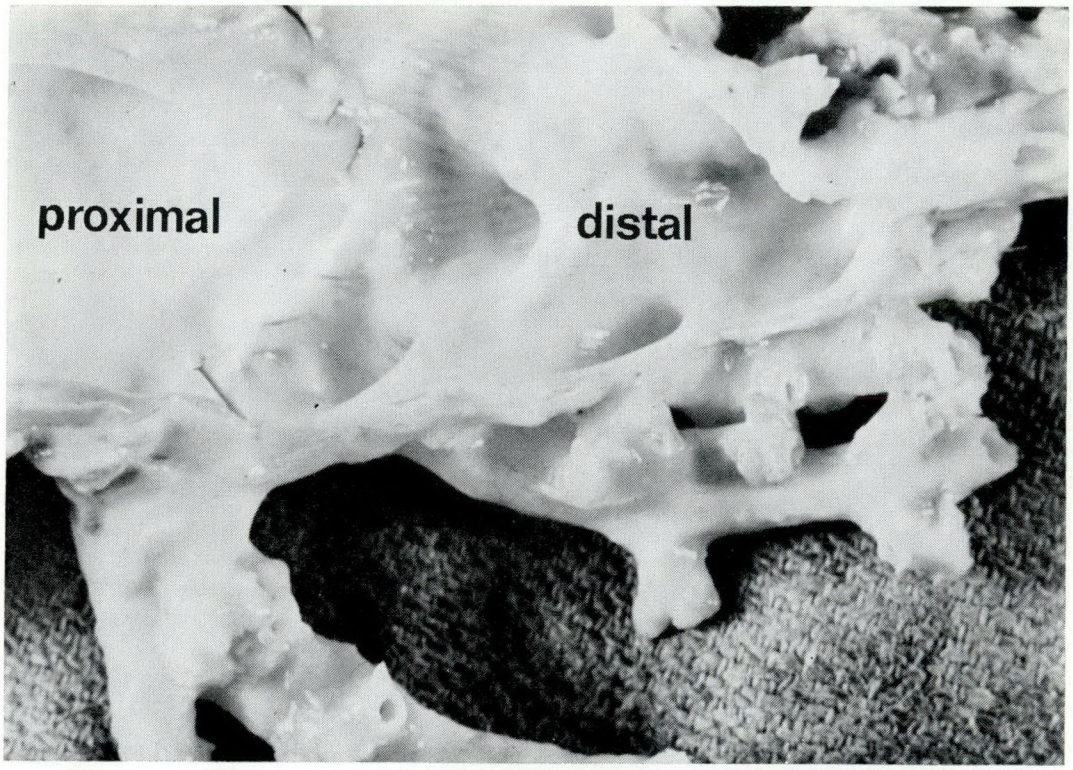

Fig. 2.—Mucosal aspect of the bronchial anastomosis in a dog killed six weeks after radical hilar stripping and division of the bronchus. In gross appearance, the mucosa distal to the suture line is normal.

tery, left main bronchus immediately proximal to the upper lobe orifice, and left atrium in that order. The vascular tree of the isolated lung was irrigated through the stump of the pulmonary artery with 500

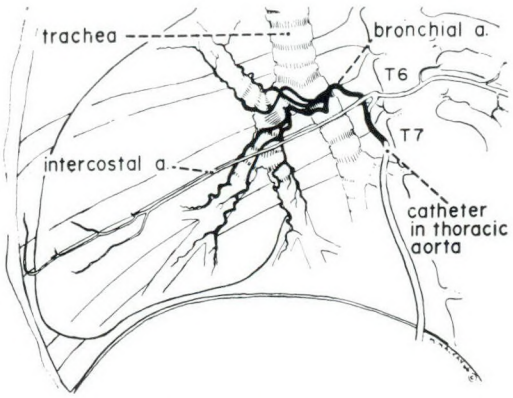

Fig. 3.—Bronchial arterial circulation in the dog. The bronchial artery commonly arises as a single branch of the fifth or sixth intercostal artery and divides, at the level of the main bronchus, into three or more branches which follow the bronchial tree to the periphery.

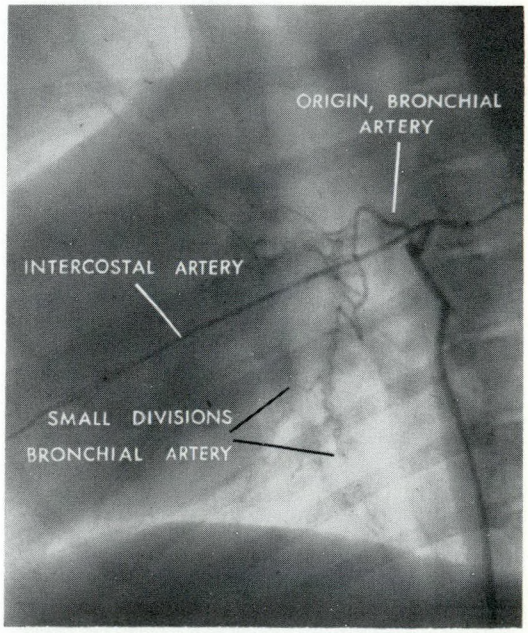

Fig. 4.—Normal preoperative bronchial arteriogram in the dog: the bronchial arterial branches clearly outline the air-containing branches of the bronchial tree.

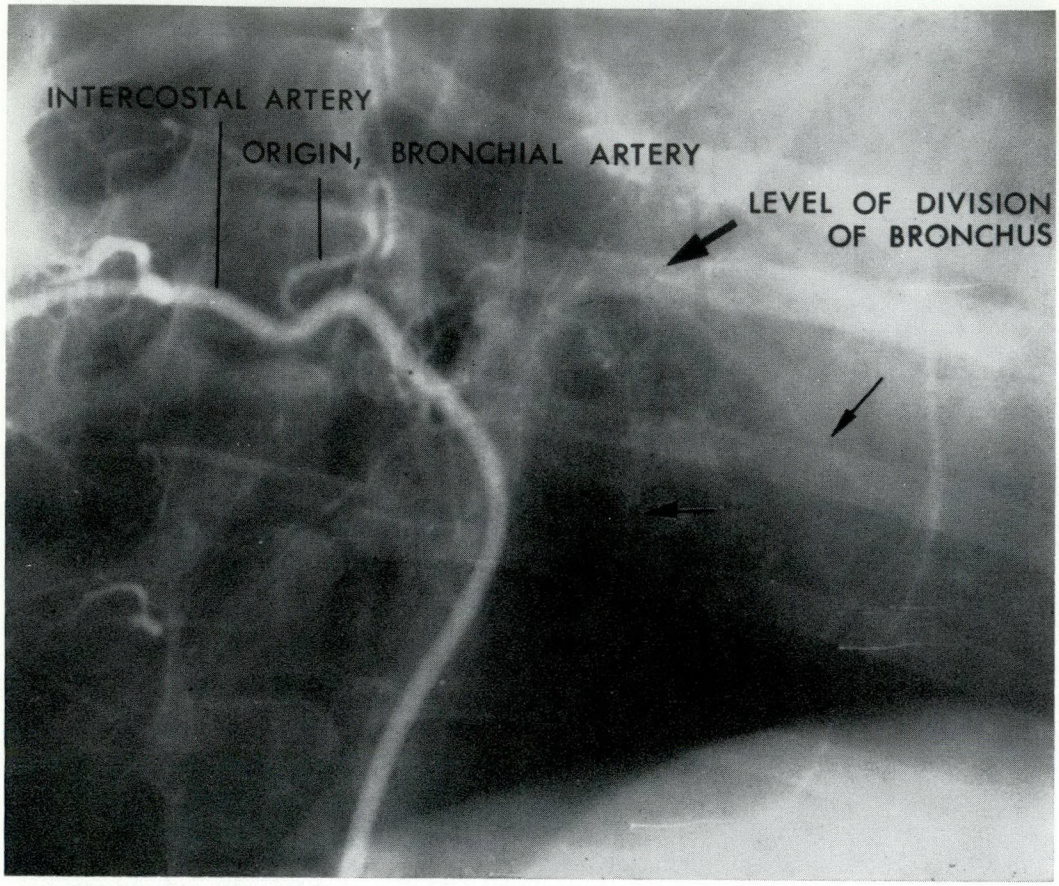

Fig. 5.—Bronchial arteriogram 43 days after radical hilar stripping. Bronchial arterial flow has been re-established in sizable arteries extending along the bronchial tree to the lung periphery (arrows).

c.c. of cool (4° C.) Ringer's lactate solution with 1 c.c. of heparin added. The lung was reimplanted and the atrial cuff and pulmonary artery were anastomosed with 6-0 silk suture. One centimetre of the proximal stump of the left main bronchus was resected and the bronchus anastomosed using a continuous 5-0 silk suture. The pleural space was drained by suction for 24 hours after operation, and intravenous tetracycline (Reverin—275 mg.) was given daily for five days after operation.

After operation, we examined these dogs at intervals by bronchoscopy, selective bronchial arteriography (Seldinger technique) and, at the time of sacrifice, by latex injection of the isolated left bronchial artery.

Results

Seven of the 15 dogs survived left lung autotransplantation and clinically remained healthy until sacrifice, between 22 and 98 days after operation. We attempted selective bronchial arteriography in the seven survivors and obtained six satisfactory arteriograms in five animals, 22 to 98 days after autotransplantation (Table I). In four dogs the origin of the left bronchial artery was successfully injected with coloured latex at thoracotomy immediately before sacrifice, 71 to 149 days after operation.

TABLE I.—Selective Bronchial Arteriography

Dog no.	*Days after operation*	*Bronchial arterial circulation*
1	(a) 22	Regeneration of many fine arterial channels at level of bronchial anastomosis. No peripheral vessels filled
	(b) 98	Totally restored to lung periphery
2	30	Restored to lung periphery, but diminished filling in distal vessels
3	33	Totally restored to lung periphery
4	41	Totally restored to lung periphery
5	43	Totally restored to lung periphery

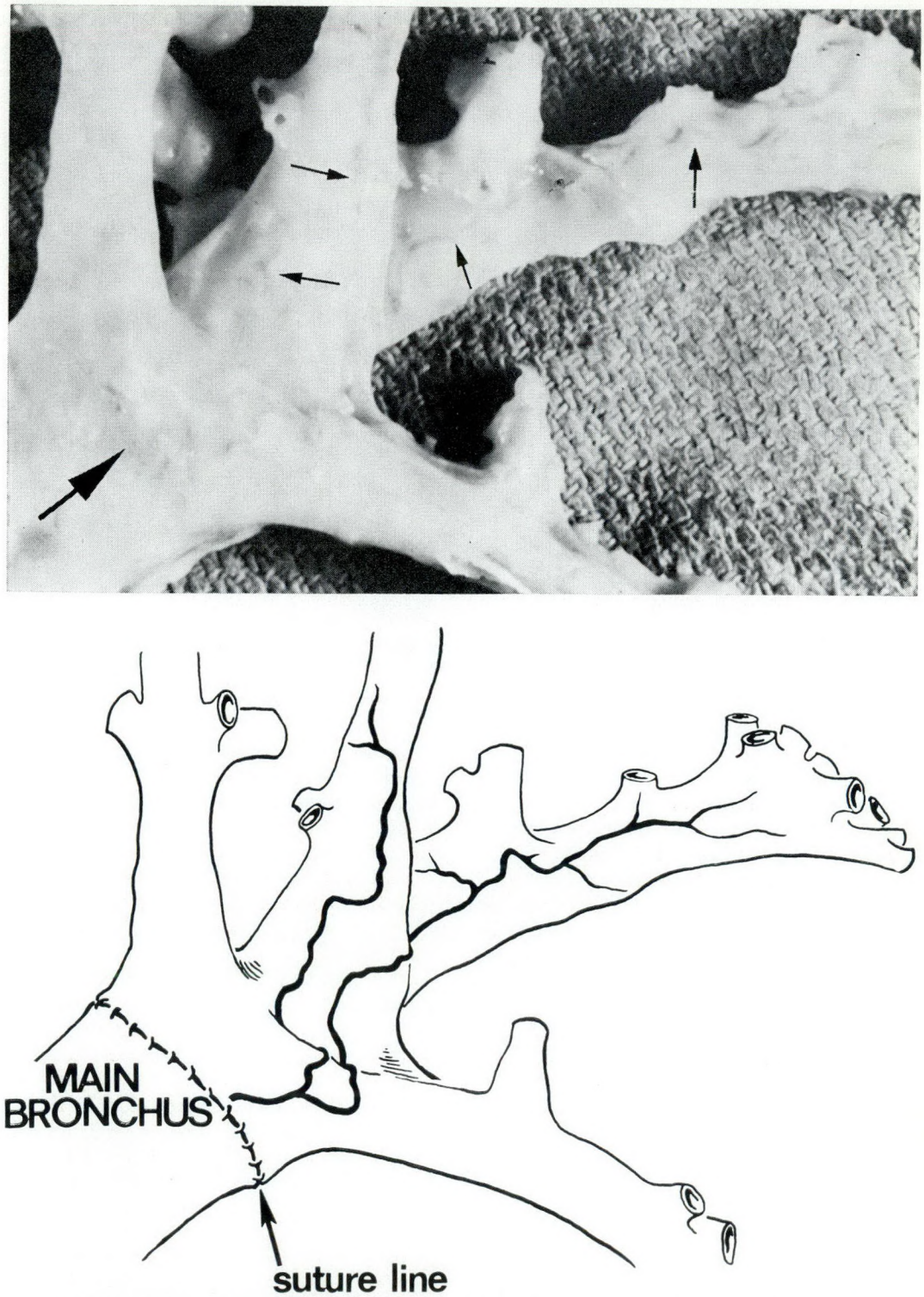

Fig. 6.—(a) Just before death the origin of the bronchial artery was injected with latex to demonstrate large vascular channels in the wall of the bronchial tree distal to the anastomosis (small arrows). The anastomosis is indicated by the large arrow. These observations are illustrated diagrammatically in (b).

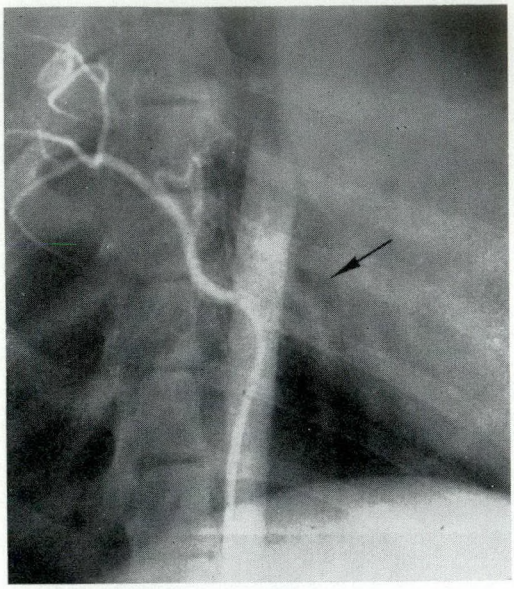

Fig. 7.—Selective bronchial arteriogram 22 days after reimplantation. A network of fine vessels has developed at the level of the anastomosis of the bronchus (black arrow), but there is no significant filling of the distal bronchial arterial channels.

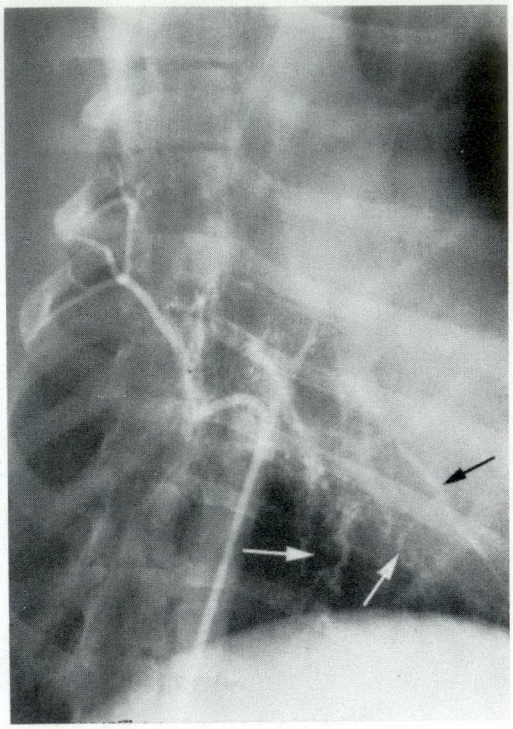

Fig. 8.—Selective bronchial arteriogram 98 days after left lung reimplantation (the same dog as Fig. 7). Vigorous bronchial arterial flow has been re-established to the periphery (three arrows).

Observations at bronchoscopy.—A bronchoscopy was done in all animals within two days of left lung autotransplantation, and at regular intervals thereafter. Our observations were similar to those recorded after radical hilar stripping and selective division of the bronchial circulation. Immediately after autotransplantation, we saw evidence of gross impairment of the circulation to the bronchial mucosa, characterized by edema, cyanosis and retained secretions distal to the anastomosis of the left main bronchus. Again, within six weeks of operation these abnormalities had completely resolved in all seven survivors.

Selective bronchial arteriography.—Before operation, bronchial arteriograms were similar in all animals (Fig. 4).

Table I summarizes observations from the successful postoperative bronchial arteriograms. In one animal, a bronchial arteriogram 22 days after operation filled a network of small arteries at the level of anastomosis of the left main bronchus, but did not fill the bronchial arteries distal to this point (Fig. 7). In this same animal, a second bronchial arteriogram 98 days after operation demonstrated total restoration of bronchial arterial flow (Fig. 8). Four other animals had successful bronchial arteriograms at 30, 33, 41 and 43 days after left lung autotransplantation. Again, the arteriogram on the thirtieth postoperative day showed that many small arteries had regenerated at the level of anastomosis of the left main bronchus, and in major bronchial arteries extending towards the periphery of the bronchial tree, flow was restored distal to this point (Fig. 9). We considered that filling in these peripheral vessels was less than normal. Arteriograms obtained at 33, 41 and 43 days after autotransplantation demonstrated an apparently complete restoration of bronchial blood flow to the reimplanted lung (Fig. 10). In these arteriograms the major bronchial arterial channels, demonstrated distal to the level of division of the left main bronchus, appeared to be the original bronchial arteries which we demonstrated in preoperative arteriograms.

Latex injection of the left bronchial artery.—Four dogs studied by latex injection into the origin of the left bronchial

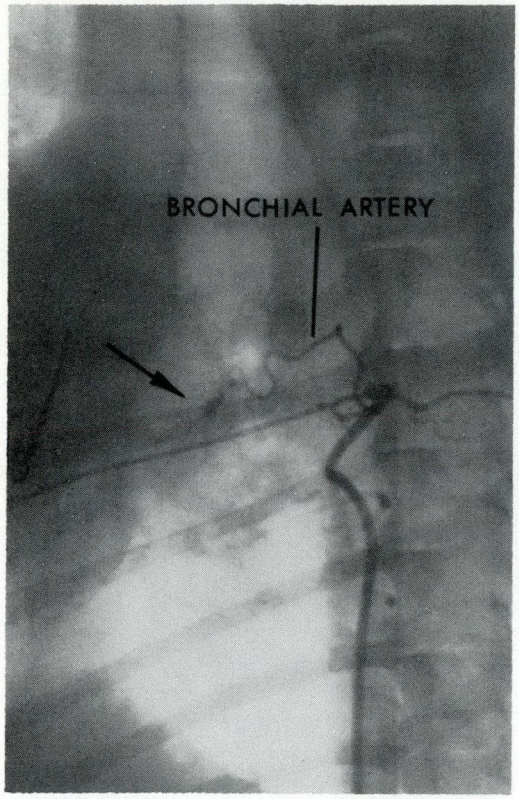

Fig. 9.—Bronchial arteriogram 30 days after left lung reimplantation showing many fine regenerating vessels at the level of the anastomosis (black arrow). Bronchial arterial channels have filled distal to this network, but this is considered to be less than normal.

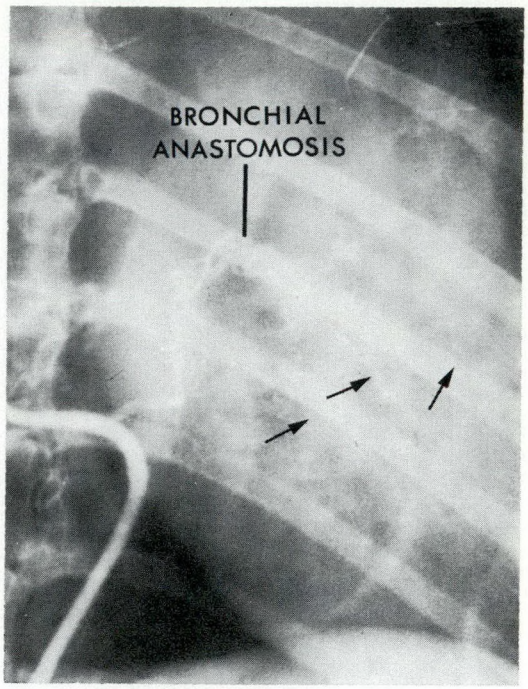

Fig. 10.—Selective bronchial arteriogram 43 days after left lung reimplantation showing a vigorous flow in arterial channels distal to the level of bronchial anastomosis (three arrows).

artery 71 to 149 days after autotransplantation had apparently complete restoration of the major bronchial arterial circulation (Fig. 6).

Discussion and Conclusions

These studies suggest that the following mechanisms contribute to restoration of bronchial arterial flow in the reimplanted canine lung: When the divided bronchus is anastomosed, the major bronchial arterial channels running in the bronchial wall on each side of the anastomosis will lie in close proximity. A network of many fine arterial channels develops and extends from the proximal cut ends of the bronchial arteries. Within three weeks of reimplantation, this network is well demonstrated by selective bronchial arteriography. Within four weeks, these fine regenerating vessels achieve effective communication with the bronchial arterial channels distal to the anastomosis. Bronchial blood flow is then re-established through the original arterial channels on the distal side of the bronchial anastomosis. During the period of small-vessel regeneration, we presume the distal bronchial arterial channels are kept patent by blood circulating from normal vascular shunts between the pulmonary and bronchial arterial vessels.

Transient impairment of the circulation in the bronchial mucosa may logically be considered the result of interrupted bronchial blood flow. On occasion, the degree and duration of this ischemia, which may be sufficient to produce necrosis, undoubtedly accounts for the stricture at the anastomosis reported in many studies of canine lung transplantation.

The accumulation and retention of bronchial mucus in the reimplanted lung may also be due to ischemic changes in the bronchial epithelium. Hypoxia stimulates increased secretion, and decreases the normal unidirectional ciliary activity. After reimplantation of the canine lung Benfield[7]

observed a significant reduction (20% to 30%) in oxygen uptake on the side of operation. This reduction was transient, tending to resolve about four weeks after reimplantation. We observed a similar alteration in oxygen uptake after the bronchial arterial circulation was divided during radical hilar stripping.[6]

Possibly the accumulation of bronchial mucus, which coincides with this defect in gas exchange, depressed oxygen uptake by producing "subclinical atelectasis" and abnormal ventilation-perfusion ratios.

These abnormalities must be considered before doing lung transplants in man. Furthermore, we have not yet determined whether or not immunologic factors will alter the pattern of bronchial artery regeneration in lung homotransplants.

Summary

In dogs, bronchial arterial circulation was studied by selective bronchial arteriography and by premortem latex injection of the bronchial artery after radical hilar stripping, and after reimplantation of the canine lung.

In both groups, the dogs re-established a vigorous bronchial arterial circulation within four weeks of its division. The mechanisms whereby bronchial arterial flow is restored are described.

Transient interruption of bronchial arterial flow is accompanied by ischemic changes in the bronchial mucosa distal to the bronchial anastomosis, and produces cyanosis and edema of the mucous membrane and the accumulation and retention of bronchial mucus. These transient abnormalities coincide with a transient defect in oxygen uptake in the reimplanted canine lung.

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Résumé

Nous avons étudié la circulation artérielle des bronches par artériographie sélective et par injection pré-mortale de latex dans l'artère bronchique après enlèvement radical du hile chez un groupe d'animaux et après réimplantation du poumon du chien dans un autre groupe.

Chez les animaux des deux groupes, la circulation artérielle des bronches a été parfaitement rétablie dans un délai de quatre semaines après sa division. Nous exposons ici les mécanismes de ce rétablissement.

L'interruption momentanée de la circulation artérielle des bronches s'accompagne de modifications de nature ischémique dans la portion de la muqueuse bronchique distale de l'anastomose bronchique, y produit de la cyanose et de l'édème ainsi que l'accumulation et la rétention de mucus bronchique. Ces anomalies transitoires coïncident avec un déficit temporaire de la fixation d'oxygène dans le poumon canin réimplanté.

METHODS IN PANCREATITIS RESEARCH USING LIVING ACINAR CELLS*

T. H. BRIAN HAIG, M.D., Ph.D., F.R.C.S.[C], *Saskatoon, Sask.*

In acute pancreatitis, etiological explanations based on extrinsic factors such as biliary reflux, ductal obstruction or vascular changes have not given us a satisfactory understanding of this unique inflammatory disease. Although some important extrinsic factor may have been overlooked, it is much more likely that we have failed to appreciate intrinsic variables that dictate the development of this disease in the susceptible individual. Individual anatomical variations have been recognized for many years, particularly in the ampullary region of the pancreas and in the major ducts within the gland. However, while preoccupied with these anatomical variations, we may have missed the nature of individual predisposition to pancreatitis rather than clarified it.

Recent progress in cellular biology has illustrated not only the contribution of molecular genetics to anatomical differences, but also a high degree of individuality in the molecular anatomy and physiology of cells. It seems unlikely that such variation could exist in cells and yet not contribute to the apparent differential susceptibility to pancreatitis. We will not gain a full understanding of the cellular determinants in acute pancreatitis using *in vivo* techniques because these lack precision, definition and are inappropriate to accurate numerical mensuration. Techniques that use cells as the basic experimental units now allow us to make quantitative experiments to differentiate between intrinsic susceptibility and extrinsic factors in the causation of pancreatitis.

The procedures described in this paper adapt common tissue-culture techniques to the solution of problems related to cellular mechanisms in acute pancreatitis. The object is to obtain fresh, living pancreatic acinar cells in suspension and test their sensitivity to several extrinsic stresses. Variations in intrinsic cellular characteristics are adjusted *in vivo* before the cells are harvested and tested.

Procedures

Procuring Fresh Living Cells in Suspension

The experimental animals are either anesthetized or killed quickly, depending upon the design of the experiment and the species used. In either case, the abdomen is opened quickly and about 5 g. of pancreatic tissue is removed and placed immediately in 15 ml. of Puck's solution* at room temperature. Excess peritoneum is removed and blood is washed away from the parenchyma. The pancreatic tissue is then transferred to 15 ml. of a solution made up just before the experiment by mixing 25 ml. of 0.02% Versene (ethylenediaminetetraacetic acid, EDTA), 25 ml. of 0.05% trypsin (1:250; Difco Laboratories, Detroit, Mich.), 50 ml. of Puck's solution and 5 mg. of powdered collagenase (*Cl. histolyticum*, supplied by Nutritional Biochemicals Corporation, Cleveland, Ohio). This mixture is brought to a pH of 7.4 just before use by adding sufficient isotonic $NaHCO_3$ with phenol-red indicator to produce an orange red colour. In this solution, the tissue is minced to 3- to 5-mm. cubes using fine scissors, and mixed in a magnetic mixer at a speed of 200 rpm and a temperature of 37° C. This mixing begins the process of tissue digestion and washes away many of the residual red blood cells. After 30 minutes, the suspension of tissue chunks and fluid is strained through four layers of clean gauze. The fluid portion is discarded and the tissue chunks are resuspended in 15 ml. of fresh

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*The formulas for, and instructions for the preparation of, Puck's solution and all of the other materials mentioned in this paragraph can be found in: Merchant, D. J., Kahn, R. H. and Murphy, W. H.: Handbook of cell and organ culture, 2nd ed., Burgess Publishing Company, Minneapolis, 1964.

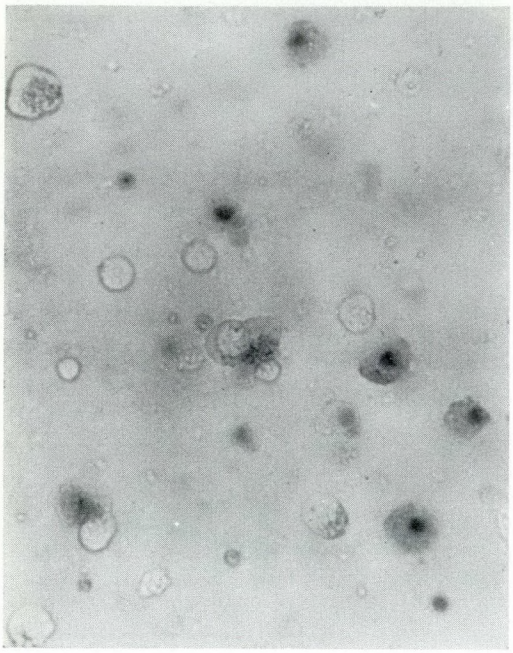

Fig. 1.—Vital staining of pancreatic acinar cells in suspension. Living cells are translucent while the nuclei and cytoplasm of the damaged cells are black.

trypsin-Versene-collagenase solution and minced further to 1- to 2-mm. cubes. The material is placed in the magnetic mixer again at 200 rpm and 37° C. for 60 minutes to digest intercellular material. This digestion frees individual living parenchymal cells which become suspended in the digestion medium. After this the material is again strained through four layers of gauze, the fluid portion containing the free living cells is retained and the tissue chunks are discarded or, if more cells are required, are digested further.

In a tube of appropriate size, the fluid portion is centrifuged at 1000 rpm and at a temperature of 5° C. for 10 minutes. The cells collect as a button on the bottom of the tube. The supernatant is quickly removed with a Pasteur pipette and the cells are resuspended in 15 ml. of Hank's balanced salt solution and centrifuged again at the same speed and temperature for a further 10 minutes. The supernatant is removed and the cells are washed once more in 15 ml. of Hank's solution. After the second aliquot of wash solution has been removed, the cells, resuspended in 20 ml. of Hank's solution, constitute the "master cell suspension" for the experiment.

Counting and Assessing Viability of Cells

Cells in suspension can be counted by one of two methods: Electronic cell counting is the most rapid method, has the least technical error and is admirably suited to cultured cells where size and type are uniform. In suspensions of cells from fresh tissue, however, the population of cells is mixed and non-cellular debris is present. This can introduce significant errors in measurement unless the instrument is programmed to count only those cells that are the size of acinar cells. Also, some toxins form a coagulum with dead cells which can plug the fine aperture through which the cells must pass to be counted. The second method, the manual hemacytometer technique, has limitations but gives satisfactory results and is the method we have used most extensively in our laboratory.

Living cells can be recognized because healthy cell membranes exclude colloidal dyes. For this work we use nigrosin (National Aniline Division, Allied Chemical and Dye Corp., New York, N.Y.), a nontoxic general protein stain made up in 0.3% solution in isotonic saline. Nigrosin (0.2 ml.) is added to 0.8 ml. of cell suspension and allowed to sit for five minutes before cell counts are made. The dye moves freely into those cells with altered membrane permeability and stains the nucleus and many of the cell organelles black. Healthy cells remain clear and refractile (Fig. 1).

Measuring Cell Integrity

To measure the ability of acinar cells to resist injury from toxic materials, we use serial dilution cytotoxicity techniques. Although dilution can be carried to any order of magnitude, we use either twofold or tenfold dilution series because they are easy to work with and to analyze. In setting up twofold dilution series, first make up a solution of test material that is sufficiently concentrated to kill all cells. Place one unit of this material in the first tube, and 0.5 units of the diluent used to

make up the test material in each of the succeeding tubes. Remove 0.5 units of full-strength material from the first tube and mix it with the diluent in the second tube. Carry this procedure on down the series of tubes and discard the extra one-half unit in the last tube. The tubes now have equal volumes of the test material in progressively greater dilutions. To each of these tubes add an equal volume of master cell suspension. After mixing, incubate the tubes at 37° C. for a fixed length of time. The appropriate length of time is determined experimentally by trial and error. We have found 20 minutes to be optimal for most of the toxins we have studied.

After incubating the cells in the test material, place the tubes in an ice bath to stop the reaction. Then add 0.8 ml. of cell suspension from each tube to 0.2 ml. of 0.3% nigrosin and make cell counts using a hemacytometer. Record the numbers of living and of dead cells for each tube and calculate the percentage of dead cells for each dilution of cell toxin. The co-ordinates for the percentage of dead cells and the logarithm of each dilution of toxin plotted on graph paper yield a straight line from which the L.D.$_{50}$ (the concentration that causes death to 50% of the cells) can be determined (Fig. 2).

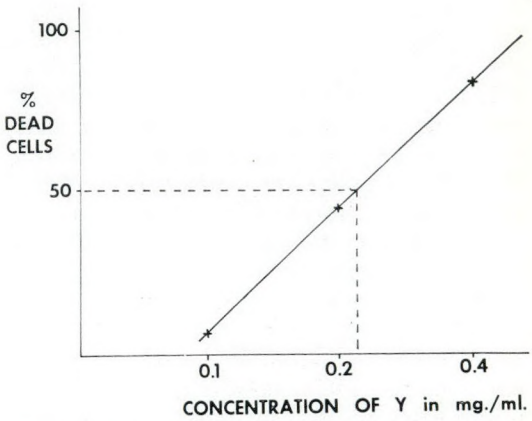

Fig. 2.—Determination of L.D.$_{50}$. The co-ordinates for the percentage of dead cells and the concentration of the particular test material are plotted on semilogarithmic paper. The L.D.$_{50}$ is determined from the resulting straight line.

Applications

These procedures can be applied to pancreatitis research in several ways: (1) The relative toxicity of various substances to pancreatic acinar cells can be determined. In this laboratory we have studied the differential toxicity of the primary and secondary bile acids in both their conjugated and unconjugated forms.[1] (2) Pancreatic acinar cells can be altered structurally or metabolically within the animal's body and the effects on cellular stability can be determined. We have done several experiments on the effect of nutritional alterations in acinar cells using these techniques.[2] (3) Interactions between a variety of cellular and extracellular variables can be assessed using this technique. For example, the integrity of cells can be altered by administering different diets or drugs to the experimental animals; the effects on the sensitivity of acinar cells to bile or other noxious agents can then be tested *in vitro*.

Because cellular alterations produced in the living animal may affect pancreatic acinar cells specifically or more generally, changes peculiar to acinar cells can be detected by doing these procedures simultaneously on cells from other organs such as liver or kidney.

Pitfalls and Limitations

Pancreatic acinar cells are inherently unstable and hence are not easily cultured. At room temperature in Hank's balanced salt solution, cellular death is continuous and progressive. However, enough cells survive for two to four hours to allow well-planned experiments. In our laboratory we have found that by incubating them in autologous serum for 10 minutes at 25° C. and washing them twice in Hank's solution the mean survival time of these cells can be prolonged for several hours. The mechanism responsible for this increased survival is not known.

The technique of manual cell counting is slow and tedious. This limits the number of experiments that can be done at one time. An automated technique for differential counting of dead and living cells in suspension, recently described by Melamed, Kamentsky and Boyse[3] might be adaptable to this work.

In the cell-counting procedure, those cells that could not exclude the colloidal dye, nigrosin, we interpreted as dead. While this is a useful designation in these experiments and in most respects is true, it is not entirely true because Kaltenbach, Kaltenbach and Lyons,[4] using several cell types, have shown that stained cells are not always metabolically dead even though they cannot reproduce. Thus, we must use caution in interpreting experiments based on vital staining techniques. However, because this technique is based on differences in cell membrane permeability, it is particularly useful in studying variations in this characteristic.

It must be emphasized that *in vitro* phenomena do not necessarily mirror biologic processes in the whole living organism. Therefore, although precise *in vitro* techniques are essential in the study of disease mechanisms at a molecular level, they must always be confirmed by appropriate *in vivo* experiments.

The procedures described in this paper do not yet have clinical applications. While they may be adapted for clinical use in the future, their real value is as a research tool and the information gained from their use will, we hope, prove to have clinical application. These methods are applicable to a number of research problems in surgery, for example, peptic ulcer and ulcerative colitis, and they point to a different way to study surgical diseases.

I wish to thank Dr. S. Fedoroff, Professor of Anatomy, University of Saskatchewan, for his advice and help in the development of these techniques, and Professor E. M. Nanson for his encouragement.

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Résumé

Diverses techniques utilisées pour la culture tissulaire ont été adaptées à l'étude des mécanismes cellulaires dans la pancréatite aiguë. Parmi ces méthodes, figuraient celles consistant dans la dislocation de tissus dans des suspensions de cellules vivantes, la numération cellulaire, la coloration vitale pour différencier les cellules vivantes des cellules mortes et les techniques d'étude de la cytotoxicité par dilution en série. L'auteur décrit ces méthodes, analyse leurs applications dans l'étude de la pancréatite et précise leurs limitations.

THORACIC-DUCT DRAINAGE BEFORE RENAL TRANSPLANTATION

Between 1966 and 1968, 50 attempts were made to drain the thoracic duct; 34 were successful. The clinical work was preceded by an anatomical study demonstrating and confirming several anatomical variations of the end of the thoracic duct at the junction with the jugular vein. The duct is approached through a transverse incision and cannulated between two valves using a Teflon tip attached to silicone rubber tubing. In the 34 successful cases, drainage was maintained for an average of 12 days, producing an average total of 18 l. of lymph. The collected lymph was centrifuged to remove the lymphocytes and the remaining fluid was reinjected. After the catheter is removed, lymph drainage usually stops spontaneously because the lymph coagulates. There were no complications such as sepsis or fistula formation. The lymphocytes were used to prepare a specific antilymphocyte serum in horses. Lymphatic drainage also depletes the lymphocytes, especially those with a long life span which play an important role in the rejection process. These lymphocytes, which are morphologically indistinguishable from the short life-span lymphocytes, are usually exhausted after eight days. For this reason, the thoracic duct should be drained for two weeks or longer in patients with small volumes of lymph.—Archimbaud, J. P. *et al.*: Technique, surveillance et intérêt du drainage du canal thoracique effectué en vue d'une transplantation rénale, *J. Chir.*, **98:** 211, 1969.

TARDY ULNAR PALSY*

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A PROGRESSIVE ulnar palsy due to a lesion at the elbow has been recognized for more than 100 years but there is still controversy regarding the etiology and best method of management in these patients. This paper describes 68 patients with progressive ulnar palsy seen at the University Hospital, Saskatoon, between 1956 and 1968, analyzing the symptomatology, investigation and treatment in an attempt to resolve the conflict regarding etiology and management.

Fifty-five of these patients were men and 13 were women. In 32, the right arm was affected and in 23 the left. In 13 the symptoms were bilateral, when they were first seen or some time later. In most patients with bilateral symptoms, both sides were affected when they were first seen, although usually some weeks passed between the onset of symptoms on one side and on the other.

TABLE I.—AGE DISTRIBUTION OF 68 PATIENTS WITH TARDY ULNAR PALSY

Age (yrs.)	*No. of patients*
21 - 30	1
31 - 40	10
41 - 50	21
51 - 60	21
61 - 70	13
Over 70	2

The majority were between 41 and 70 years of age, the youngest was 25 and the oldest 73. The mean age was 51 years (Table I). The ages of those patients with ulnar palsy following severe trauma to the elbow in childhood varied from 25 to 63 with a mean of 42 years. On the other hand, those patients with osteoarthritis of the elbow varied in age from 50 to 71 with a mean age of 60. Of the group of patients where the ulnar nerve lesion occurred with a normal elbow, the age ranged from 36 to 61 with a mean of 52.

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TABLE II.—TARDY ULNAR PALSY. DURATION OF SYMPTOMS

Duration	*No. of patients*
Less than 1 mo.	5
1 - 3 mos.	13
3 - 6 mos.	14
6 - 12 mos.	11
1 - 5 yrs.	13
Over 5 yrs.	10

DURATION OF SYMPTOMS

Almost one-half the patients had suffered for less than six months; the shortest duration was three weeks and the longest 30 years (Table II). Two patients had symptoms for 30 years and one for 29. Two other patients had complaints for many years but could not be specific.

ASSOCIATED OR PRECIPITATING FACTORS

Severe trauma to the elbow as a child (Table III).—Twelve patients had severe trauma and fractures at the elbow as a child; in seven of these, the resulting deformity was confirmed by radiographs. Cubitus valgus was present in seven and fixed flexion deformities in four. These deformities are not necessarily exclusive and, indeed, the fixed flexion or limitation of extension always occurred in association with cubitus valgus.

Osteoarthritis (Table III).—Other than post-traumatic arthritis, the elbows of 13 patients showed definite degenerative arthritic changes; these were minimal in four but gross in nine. Of these 13, one had cubitus valgus and two had fixed flexion deformities. One other patient had a loose

TABLE III.—ASSOCIATED CONDITIONS IN PATIENTS WITH ULNAR PALSY

		No. of patients
Severe trauma as a child		12
radiographs showing old trauma, arthritis	7	
cubitus valgus	7	
fixed flexion deformity	4	
Arthritis of elbow		13
minimal changes	4	
gross changes	9	
fixed flexion deformity	2	
loose body in joint	1	
cubitus valgus	1	

body removed from the elbow joint.

Injury to the elbow before the onset of symptoms.—Six patients had minor injuries to the elbow before symptoms began. Several felt paresthesia immediately; in others the symptoms may have been delayed for a few days.

Onset associated with flexion of the elbow.—In eight patients the symptoms began after the elbows were flexed for a long period. One, who had been attending a study course, spent much time with his elbows on the desk and his chin in his hands. Another had been playing a lot of chess in a similar position. One patient had been using elbow crutches and five others, confined to bed because of other conditions, had spent much time on their backs with their hands folded across their chest.

Other trauma.—Two patients described trauma to the hand just before their symptoms began, although the nerve lesion was definitely at the elbow.

Previous episodes.—Only one patient had a previous episode of ulnar paresthesia: it had cleared spontaneously.

Other associated conditions.—Six patients had associated conditions, some of which may have contributed to the ulnar palsy, *viz.* torsion dystonia, parkinsonism, diabetes mellitus, acromegaly, poliomyelitis with kyphoscoliosis, and schizophrenia (each patient had only one condition).

Symptoms (Table IV)

Of the 68 patients, 65 had sensory symptoms and either paresthesia or numbness on the ulnar border of the hand.

Forty-two patients had weakness of the hand and many gave this history only when asked specifically; this symptom was not volunteered as were the sensory symptoms.

TABLE IV.—Symptoms in Patients With Tardy Ulnar Palsy

Symptoms	*No. of patients*	*No. of hands*
Numb only	13	18
Numb and weak	20	24
Numb and painful	12	13
Numb, weak and painful	20	20
Weak only	0	0
Weak and painful	2	3
Pain only	1	2

TABLE V.—Clinical Findings

Signs	*No. of patients** *Mild*	*Moderate*	*Severe*
Sensory	11(5)	50(4)	5 (1)
Wasting	10(4)	34(3)	14 (2)
Weakness	13(5)	41(4)	10 (1)

Flexor carpi ulnaris involved in 5
Swollen nerve in 40
Dislocating nerve in 1

*Numbers in brackets denote patients with bilateral findings.

Thirty-five had pain usually around the elbow. It was not well localized and sometimes spread upwards or downwards and was occasionally felt on the ulnar border of the hand. If one counts patients with bilateral symptoms as separate limbs, then 75 limbs had sensory symptoms, 47 weakness and 38 pain.

Of course, a number of patients had several symptoms and none complained of weakness alone. Only one complained only of pain and two complained only of weakness and pain. The rest all had sensory symptoms, 13 had no other complaints, 20 had associated weakness, 12 had associated pain and 20 had both pain and weakness. In association with the weakness, some of these patients noticed wasting of the hand, particularly of the first dorsal interosseus.

Clinical Findings (Table V)

Of the 68 patients, 66 had sensory impairment in the ulnar distribution; it was minimal in 11, moderate in 50 and severe in five. Fifty-eight patients had wasting of the intrinsic muscles of the hand, particularly the first dorsal interosseus; in 10 it was minimal, and in 14 severe.

Sixty-four had weakness of the ulnar-supplied intrinsic muscles; in 13 this was minimal, but in 10 it was severe.

We usually palpated the ulnar nerve at the elbow and in 40 instances considered that the nerve was swollen. In the patients' records nerve dislocation was mentioned only once.

Only five patients had involvement of the flexor carpi ulnaris according to the records.

Diagnostic Studies (Table VI)

Electromyography and nerve conduction studies were done on many of these pa-

TABLE VI.—Diagnostic Studies

	*No of patients**
Electromyography	
Abnormal	36 (1)
Normal	10 (2)
Nerve conduction studies	
Abnormal	22 (2)
Normal	9 (2)

*Numbers in brackets are patients in whom studies were done bilaterally.

tients and sometimes repeated after treatment. The electromyogram was definitely abnormal in 36 of 46 patients. In three with bilateral lesions, the electromyogram was abnormal in one and normal in two.

Nerve conduction studies were done in 31 patients, four of whom had bilateral lesions. In 22 patients (24 limbs) nerve conduction in the region of the elbow was slowed, but this was normal in nine patients (11 limbs).

Treatment

Eleven patients had no treatment because their symptoms were minimal or were improving when they were first seen. Three other patients refused operation. We have no follow-up in seven of these 14 patients, but of the other seven, four have no symptoms and three are considerably improved (Table VII). Of the seven who have been followed-up, only one has a completely normal hand, but in six the ulnar lesions have improved considerably. The length of follow-up in these seven patients is one year in four, two years in two, and three or more in one.

Transposition Operations (Table VIII)

In 11 patients, the ulnar nerve was transposed to the front of the elbow; in two, this was done before they were seen at the University Hospital. Ten of these 11 said their symptoms had improved—three had no symptoms at all. One patient said that he was worse. On examination, however, only two patients had normal

TABLE VII.—Results in Patients With No Operation

	Symptoms	*Signs*
Normal	4	1
Improved	3	6
Unchanged	0	0
Worse	0	0

TABLE VIII.—Results of Transposition Operations

	Symptoms	*Signs*	*Electromyography*
Worse	1	1	0
Unchanged	0	1	0
Improved	7	7	3
Normal	3	2	0

hands, but seven others were quite definitely improved, one probably had the same signs as before operation and one was worse. Repeated electromyography in three patients showed definite improvement in all. The length of follow-up was one year or less in seven, and in the other four was three, four, five and 10 years respectively.

Decompression Operations (Table IX)

Fifty-four decompression operations were done in 50 patients; two of these also had epicondylectomy. In this discussion, each operation is considered as a separate event, i.e. bilateral procedures count as two procedures. Sixteen hands were normal at follow-up, 25 improved, eight unchanged, three worse and two unknown. All these patients (except two who were lost to follow-up) have been examined and 11 have no abnormal signs, 31 are definitely improved, six are probably stationary, and four are worse. The electromyogram was repeated in 13 patients; it was normal in six, improved in four, unchanged in two and worse in one. For 28 hands, the length of follow-up is one year, for 12 two years, and for 12 three or more years.

Three of the patients first seen by our staff had operations elsewhere. In one, a decompression produced no improvement. Two others had transposition and both had some improvement.

Reoperations

In 1959 one patient had a transposition elsewhere with little improvement. In 1960

TABLE IX.—Results of Decompression Operations

	Symptoms	*Signs*	*Electromyography*
Worse	3	4	1
Unchanged	8	6	2
Improved	25	31	4
Normal	16	11	6

he had neurolysis at the same hospital with no improvement, and a further neurolysis in 1962 at the University Hospital with perhaps some slight improvement.

One patient had a decompression in 1963, but because he deteriorated after initial improvement had a transposition in 1966. Now after one year he has approximately 75% recovery.

One patient had the ulnar nerve explored in 1956 at another hospital, then the brachial plexus was explored, and finally the nerve was decompressed at the University Hospital in 1958. After this last procedure, he has had some improvement.

Another patient, who had a decompression in 1966 and some progression of his signs in the summer of 1968, was readmitted for ulnar transposition in January 1969. Three months later his condition had not changed.

Bilateral Procedures

Five patients had bilateral procedures. One had a transposition done elsewhere in 1950, and a decompression on the other arm done at the University Hospital. He had improvement on both sides. One woman, who had bilateral decompression in 1964 several months apart, committed suicide six months after the second operation. However, at the time of her death she had some improvement in both ulnar palsies.

A third patient who had bilateral decompression in 1960, had no symptoms two years later but still had some residual signs.

A fourth patient who had ulnar decompression on one side in 1966, had 90% recovery two years later. He had a decompression on the opposite side one year later, had 90% recovery in 18 months, but deteriorated again. He was readmitted and a transposition done in January 1969; three months later he had no change in his ulnar palsy.

The fifth patient, who had a decompression in 1956, had 90% symptomatic and clinical recovery over a period of eight years. We did a decompression on the other side in 1962 and this hand was normal two years later.

Deaths

Three of these patients have died, one from suicide (this was not related to the ulnar palsy), one from cancer and one in an accident.

Discussion

For many years, physicians have recognized a progressive ulnar nerve lesion not associated with open trauma. According to Arkin,[1] Blattman in 1851 described such palsy associated with subluxation of the ulnar nerve out of the groove behind the elbow. Gowers[2] described a compression neuropathy in 1866, and Panas[3] in 1878 described ulnar palsy unassociated with dislocating nerve, under the term "ulnar neuritis". This progressive ulnar lesion has been attributed to many causes (Table X).

TABLE X.—Causes of Progressive Ulnar Lesions

1. Local trauma and contusion of the nerve.
2. A dislocating nerve damaged during its passage to and fro across the medial epicondyle and perhaps more liable to local injury.
3. A shallow ulnar groove which tends to dislocation and trauma.
4. A cubitus valgus deformity of the elbow—the ulnar nerve is stretched around the inner side of the elbow.
5. Limited extension of the elbow—the nerve is continually stretched around the posteromedial aspect of the elbow.
6. Old trauma, particularly in childhood, resulting in cubitus valgus deformity, fixed flexion deformity and traumatic osteoarthrosis.
7. Recent fractures of the medial epicondyle.
8. Recurrent dislocation of the elbow.
9. Local osteoarthrosis—the nerve may rub against osteophytes.
10. Rheumatoid arthritis—the nerve may be compressed by granulomatous tissue around the joint.[16]
11. Other forms of arthritis, e.g. tuberculous arthritis.
12. Neuropathic arthritis secondary to syringomyelia,[4] although it may be difficult to differentiate between the signs and symptoms of syringomyelia and those of ulnar palsy.
13. Ganglia and bursae around the elbow joint.
14. Hypermobile elbow joints and cubitus recurvatus.[17]
15. Pressure on the inner side of the arm, mentioned in bed patients, particularly unconscious patients.[8, 9]
16. Scarring and constriction of the nerve following local injury.
17. Occupational trauma—repeated pressure on the elbow produces adhesions of the ulnar nerve in the groove.
18. Anomalous muscles or vessels crossing the nerve in the region of the epicondylar groove.
19. Foreign bodies or tumours.

In a preliminary communication to the British Orthopaedic Association in 1957 and in a paper in 1959, Osborne[4] suggested that in progressive ulnar palsy the nerve is compressed by the two heads of flexor carpi ulnaris—the fibrous band bridging these two heads becomes slack in extension and tightened in flexion. When the elbow is flexed this tightening diminishes the space between the fibrous band and the immediately subjacent elbow joint. However, Feindel and Stratford[5] were thinking along the same lines; their first cases were operated on in April and October 1956, although they did not publish their findings until 1958 and later in a longer paper.[6] The first of these papers shows that these authors were aware of Osborne's work. Nicolle and Woolhouse in 1965[7] described a similar mechanism.

The clinical features in our patients differ little from those described in the literature. There is usually a male preponderance, the right side is affected more often than the left, and bilateral lesions are common. The average patient is about 50 years of age and most patients are between 40 and 70 years. Duration of symptoms varies; most patients present within a year of the onset of symptoms, but many have complaints for much longer. The symptomatology in our patients does not differ from those described in the literature. The most common symptom is numbness; weakness and pain are less frequent and, of course, combinations of these three symptoms are common. On examination, sensory signs are the most common but wasting and weakness are frequently seen. The association of childhood trauma to the elbow and the late development of ulnar palsy is well known; nearly 20% of those in the present series had this association—a figure that is somewhat lower than in many series. The association of ulnar palsy and degenerative and other forms of non-infective arthritis also occurred in 20% of patients. Thus, 60% of these patients had normal elbows, and only six (15%) had a minimal local trauma that might have precipitated their symptoms. In view of the delayed onset in these patients, symptoms may have followed changes in the cubital tunnel, e.g. edema or hemorrhage into surrounding muscle or ligamentous tissue rather than direct trauma to the nerve itself. In the remaining 45%, repeated flexion and extension of the elbow may have precipitated the ulnar palsy. Ulnar palsy associated with prolonged illness and bed rest have been reported by Humphreys and Karavitis,[8] Estridge and Smith,[9] and Gowers.[2] People whose elbows rest on the table, although formerly accused of compressing the ulnar nerve at the elbow, probably constrict the cubital tunnel by flexion. As one gets older, transient ulnar palsy after a period of elbow flexion is common, but this usually passes in a matter of minutes.

In the past, involvement of the flexor carpi ulnaris has been said to imply a lesion higher than the two heads of the flexor carpi ulnaris because the branch to this muscle comes off more proximally. This is not always true because the branch to the flexor carpi ulnaris runs with the ulnar nerve in the cubital tunnel or indeed may come off in the cubital tunnel, so that, even with the cubital tunnel syndrome, the flexor carpi ulnaris may be involved on occasion. In nearly two-thirds of the patients in this series, the ulnar nerve in the epicondylar groove was enlarged on palpation. Although attributed to irritation caused by subluxation, traction over the elbow joint, or pressure over osteophytic projections, this enlargement probably represents typical nerve swelling above a constricting lesion. Nerve dislocation was reported in only one patient in this series.

Ashenhurst[10] in 1962 examined 300 patients who had no ulnar nerve lesions and showed that 22% had mobile ulnar nerves, although in only 3% did the nerve dislocate completely. Childress[11] in 1956 examined 2000 ulnar nerves and found that 16.2% dislocated completely or incompletely. In three-quarters of these, the dislocation was incomplete and was usually bilateral. The actual contribution of nerve dislocation to tardy ulnar palsy is uncertain, but probably only contributes by subjecting the nerve to more trauma when the elbow is flexed.

In patients with peripheral nerve lesions, electromyography and particularly nerve conduction studies delineate the site of the

TABLE XI.—Traumatic Arthritis: Results With Two Procedures

	Transposition	*Decompression*	*No operation*
Worse	0	1	0
Unchanged	0	0	0
Improved	4	3	0
Full recovery	2	1	0
No follow-up	0	0	1

TABLE XII.—Osteoarthritis of Elbow: Results With Two Procedures

	Transposition	*Decompression*	*No operation*
Worse	0	0	0
Unchanged	1	2	0
Improved	0	6	0
Full recovery	0	3	0
No follow-up	0	0	1

obstruction to the flow of nerve impulses.[12, 13] Of 35 such studies in the present series, 24 were abnormal, confirming that the lesion was just below the elbow. These studies are a useful part of the follow-up because changes may be seen before any obvious clinical improvement and preoperative and postoperative findings can be compared.

With respect to treatment, some patients with ulnar palsy may be improving when first seen so that spontaneous recovery does occur. In this series, seven patients who were followed-up all improved without operation, although only one has no abnormal residual signs.

Historically, the first operation for tardy ulnar palsy was fixing the dislocating ulnar nerve back into its groove. This was soon superseded by transposition in which the nerve was moved from behind the elbow to the front placing it in muscle or under the skin. In association with this, some surgeons removed the medial epicondyle and part of the supracondylar ridge. Following the reports of Osborne, and Feindel and Stratford, simple decompression procedures have become popular—the fibrous band joining the two heads of flexor carpi ulnaris is divided over a sufficient length to relieve the nerve at the site of obvious compression. Sometimes the medial epicondyle is also removed, although this is probably unnecessary. In 1966 Gore and Larson[14] recommended medial epicondylectomy for subluxing ulnar nerves and claimed improvement in all 14 patients so treated. In 1959 King and Morgan[15] described epicondylectomy in the management of this condition.

In the present series of patients, transposition was done in only 11, 10 were improved and one became worse. Nerve decompression was done 54 times in 50 patients with improvement in 42, no change in six and probably some worsening in four. Some patients had several operations: one after a transposition, two after earlier decompressions (the second procedure was then a transposition) and in one, the ulnar nerve was explored in the mid-forearm and later decompressed. In three of these patients who have been followed, only one had considerable recovery. Although 13 patients had bilateral ulnar lesions, only five had bilateral procedures.

Tables XI and XII compare the results of transposition and decompression in patients with post-traumatic arthritis or degenerative osteoarthritis. In those with traumatic arthritis, six had transposition, five decompression, and one no operation. This last patient was not followed. All patients who had transposition improved or made a full recovery. Only four of the five who had decompression procedures had improvement, and only one of these had full recovery, the other was made worse.

Only one patient with osteoarthritis of of the elbow had transposition; he had little or no change in his palsy. Eleven were decompressed: nine improved considerably (three made a full recovery) and only two were relatively unchanged. One had no operation and was not followed (Table XII).

Table XIII shows those patients who had an apparently normal elbow, except for the ulnar nerve lesion. Four were treated by transposition; three had improvement, and one had some worsening. Thirty-six were treated by decompression: 29 made a good recovery and seven of

TABLE XIII.—Normal Elbow: Results With Two Procedures

	Transposition	*Decompression*
Worse	1	3
Unchanged	0	4
Improved	3	22
Full recovery	0	7
No follow-up	0	0

these returned to normal. Three became worse after decompression.

These results suggest that transposition is less likely to make the patient's condition worse. The operative notes on one patient suggest that transposition is a better procedure in post-traumatic arthritis of the elbow, and perhaps when the patient has severe degenerative arthritis with a fixed flexion deformity. This patient had two very definite areas of nerve constriction—one where the two heads of flexor carpi ulnaris joined, and the other where the nerve passed through the medial intermuscular septum above the elbow. Obviously constriction at the medial intermuscular septum cannot be treated by simple decompression.

In tardy ulnar palsy without evidence of deformity around the elbow, the correct procedure is decompression of the nerve where it passes between the two heads of the flexor carpi ulnaris. Patients with degenerative arthritis associated with a fixed deformity or cubitus valgus deformity require transposition of the ulnar nerve. Those who have tardy ulnar palsy after an old elbow injury in childhood should also have transposition.

The satisfying response after decompression of the nerve in the cubital tunnel suggests that this lesion is due to entrapment neuropathy as suggested by Osborne, and Feindel and Stratford.

Summary

At the University Hospital, Saskatoon, 68 patients with slowly progressive ulnar palsy were treated by nerve transposition or decompression. The author describes the results of different forms of treatment and discusses the role of transposition of the nerve and decompression in the cubital tunnel. The findings at operation and the results obtained with decompression confirm that tardy ulnar palsy is due to entrapment with compression of the nerve in the cubital tunnel.

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Résumé

A l'Hôpital Universitaire de Saskatoon (Saskatchewan), on a traité 68 malades souffrant de paralysie cubitale à évolution lente, par transposition nerveuse ou par décompression. L'auteur analyse les résultats des divers modes de traitement et précise le rôle de la transposition du nerf et de la décompression dans le canal du nerf cubital. Les constatations peropératoires et les résultats obtenus par la décompression confirment que la paralysie cubitale lente est causée par l'emprisonnement du nerf dans le canal cubital où il est comprimé.

IDIOPATHIC HEMOCHROMATOSIS PRESENTING AS "ACUTE ABDOMEN": A REPORT OF TWO CASES*

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In idiopathic hemochromatosis, because of an inborn error in iron metabolism, normal storage proceeds to an extreme degree. The accumulation of excess iron as ferritin and hemosiderin gives rise to fibrosis and failure of function of the involved organs.

Clinically the disease is characterized by cirrhosis of the liver, skin pigmentation, diabetes mellitus and endocrine dysfunction. A significant number of these patients do not, however, conform to this pattern, and even after careful observation and investigation the disorder may not be recognized. In some patients the sole presenting symptom may be abdominal pain and, occasionally, this may be severe and difficult to differentiate from that associated with common surgical emergencies.[1] For this reason patients with undiagnosed idiopathic hemochromatosis will, from time to time, be admitted to surgical units.

The two cases described in this paper focus attention on idiopathic hemochromatosis as a cause of undiagnosed abdominal pain and illustrate some specific problems in diagnosis and management that these patients present to the surgeon.

Case Reports

Case 1.—A 68-year-old man was admitted to hospital in November 1962 complaining of right-sided upper abdominal pain and bile-stained vomiting of two days' duration. The pain, which was steady, had become very severe two hours before admission. His general health had been good and he had had no previous gastrointestinal symptoms.

On examination he was tender in the right hypochondrium, and had local guarding and release tenderness. No other abnormality was noted. His blood pressure was within normal limits. His hemoglobin was 14 g./100 ml., leukocyte count was 6000/c.mm., serum amylase was less than 160 Somogyi units, the urine contained neither sugar nor albumin, and a flat plate of the abdomen did not demonstrate any opaque gallstones. Standard tests of liver function were all within normal limits.

On a provisional diagnosis of acute cholecystitis of intermediate severity, the patient was treated with bed rest, analgesics and oral fluids. On this regimen his symptoms settled down within a few hours, although the localized abdominal tenderness remained for two days. Three weeks later, on oral cholecystography, the gallbladder outlined very faintly, no gallstones were seen, and the dye did not concentrate a fatty meal. We advised cholecystectomy but the patient refused. During the succeeding three months he had further attacks of right hypochondrial pain which were never severe and were relieved by analgesics and bed rest. He had one severe attack of pain in February 1963 and after this he requested cholecystectomy. He was admitted for operation in April 1963.

Investigations before operation were not significantly different from those in November 1962.

At operation the gallbladder and extrahepatic ducts appeared normal. There was no evidence of previous inflammation. No gallstones were palpable within the gallbladder or in the ducts. The rust brown liver was slightly enlarged and mildly cirrhotic. The spleen was slightly enlarged. After biopsy of the liver had been taken, we closed the abdomen. His recovery was uneventful.

Subsequently the liver biopsy was reported as showing the typical features of hemochromatosis. His glucose tolerance test was within normal limits. The plasma iron was 200 μg./100 ml. (normal, 80 to 150 μg./100 ml.) and the total plasma iron binding capacity was 300 μg./100 ml. (normal, 300 to 400 μg./100 ml.).

This patient was treated by repeated venesections. At cholecystogram one year later his gallbladder functioned normally. He had had no further episodes of abdominal pain since treatment began. When he was last seen, in 1968, he was well.

Case 2.—A 56-year-old woman was admitted to hospital in February 1964 complaining of lower right-sided abdominal pain of two hours' duration. The pain, which began suddenly,

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was initially felt across the lower abdomen but localized to the right iliac fossa shortly before admission. In 1959 she had been admitted to hospital with a similar, but not so severe, attack of pain. Barium enema at that time had not demonstrated any abnormality. For several years she had been treated with steroids for rheumatoid arthritis. These treatments, however, had been stopped in 1962.

On examination, the patient was tender across the lower abdomen and had maximal tenderness in the right iliac fossa where there was guarding and release tenderness. Her blood pressure was 150/80 mm. Hg. Her hemoglobin was 15 g./100 ml., leukocyte count was 12,000/c.mm., serum amylase less than 160 Somogyi units, the urine was clear and contained neither albumin nor sugar. A flat plate of the abdomen revealed no abnormality. Serum electrolytes and urea were normal.

The patient continued to complain of abdominal pain and, with a provisional diagnosis of acute appendicitis, her abdomen was explored through a lower right paramedian incision eight hours after admission. The appendix and other abdominal organs were normal except the liver which, although of normal size, was mildly cirrhotic and rust brown. Her appendix was removed and her abdomen closed. Because of the previous history of steroid therapy she was covered with steroids. At the end of the operation, her blood pressure was 130/85 mm. Hg and her pulse rate was 88/min.

Her immediate recovery was satisfactory, but after four hours her blood pressure began to fall and her pulse rate increased. An intravenous infusion was set up and, in turn, we infused one litre of normal saline, hydrocortisone, blood and metaraminol bitartrate (Aramine) without effecting any improvement in the falling blood pressure. An electrocardiograph did not show any evidence of myocardial infarction. Her blood pressure continued to fall and she died 15 hours after operation.

At post mortem, no immediate cause of death could be found. The appendiceal stump was intact. The thyroid gland, the heart, the liver and the pancreas were rust brown in colour. The liver was mildly cirrhotic and slightly enlarged. On subsequent histologic examination these tissues demonstrated the typical changes of hemochromatosis. All other abdominal and pelvic organs including the adrenals were normal.

Discussion

In these two patients the presenting symptom of idiopathic hemochromatosis was severe abdominal pain, as in several published reports.[1-3] In these circumstances, the site and quality of the pain may vary from case to case and consequently this disorder may simulate a variety of intra-abdominal emergencies.

Various theories have been advanced to explain this pain. Because the crises of Addison's disease may be heralded by gastrointestinal manifestations, including abdominal pain, Desforges[1] has suggested that, in idiopathic hemochromatosis, the gradual deposition of iron within the adrenal glands may finally produce adrenal cortical insufficiency. As in Addison's disease the final crisis may be precipitated by any mild stress. Clinically, however, there is only a superficial resemblance between these two conditions. Furthermore, intravenous hydrocortisone, while of great value in an Addisonian crisis, is completely ineffective in idiopathic hemochromatosis complicated by abdominal pain and profound shock. Patients with idiopathic hemochromatosis may develop congestive cardiac failure secondary to iron deposition within the myocardium, particularly when the disease manifests itself before 40 years of age. Because the right ventricle cannot deal with the venous return the liver enlarges and, in the early stages, the patient may have pain in the upper abdomen from stretching of the liver capsule. This pain, however, bears little resemblance to the crisis-like pain of hemochromatosis. Furthermore hemochromatotic patients who die following an abdominal crisis do not have evidence of congestive heart failure at post mortem.

About 80% of patients with idiopathic hemochromatosis develop diabetes mellitus.[4] In unrecognized, and therefore uncontrolled, diabetes the patient may have symptoms suggestive of gastrointestinal disease such as nausea, vomiting and abdominal pain. In diabetic acidosis, the pain may be severe and in many ways simulate an acute intra-abdominal emergency. There are many points of similarity between the abdominal pain of diabetic

acidosis and the abdominal crisis of idiopathic hemochromatosis. However, patients with idiopathic hemochromatosis presenting with abdominal pain rarely have associated diabetes mellitus. One such patient who presented with severe pain in the limbs and abdomen had deposits of iron within the peripheral nerves.[5] Such findings may explain why these patients have pain, but it does not account for the frequent, sudden, and often localized abdominal pain.

Hypotension

The patient in Case 2 died from progressive irreversible hypotension. Irreversible shock may occasionally be associated with the abdominal pain of idiopathic hemochromatosis.[1, 6, 7] Recently it has been suggested that this progressive hypotension is due either to ferritin release or endotoxemia.

The iron-bearing protein, ferritin, which is constantly present in the blood of patients with irreversible hypotension,[8] may have been released into the circulation by the hypoxic liver.[9] Initially it was believed that ferritin exerted its effect by directly paralyzing the smaller blood vessels, but recent studies have shown that ferritin acts indirectly by rendering intravascular vasoconstrictor material inert,[10] and thus producing vasodilation. Because patients with idiopathic hemochromatosis have increased depot and circulating ferritin, the irreversible hypotension found occasionally in these patients has been widely attributed to "ferritin shock". However, this thesis can only be accepted with reservation because one cannot induce hypotension in experimental animals by injecting ferritin intravenously[11] even after hepatectomy and nephrectomy (such animals can neither metabolize nor excrete ferritin and hence should have been extremely susceptible to its action). More recently it has been shown that although levels of plasma-bound iron are consistently increased in hemorrhagic shock, increased levels are not found consistently in several forms of normovolemic shock. Plasma-bound iron levels usually fall in shock that is not due to blood loss.[12]

Bacterial Endotoxins

Fine[13] believes that the principal defect in progressive shock is the reticuloendothelial system's failure to detoxify circulating endotoxins. Normally, bacterial endotoxins, elaborated in the bowel lumen by gram-negative bacteria, are absorbed into the portal circulation and quickly destroyed by the reticuloendothelial system within the liver. When reticuloendothelial activity is depressed, as in shock, bacterial endotoxins accumulate within the host, depress the smaller blood vessels, converting them into atonic channels that hold increasing volumes of blood. This vasodepression produces a progressive decrease in effective circulating blood volume, progressive hypotension and finally death. Experimental studies[14, 15] have demonstrated that the intact reticuloendothelial system protects against the harmful effects of endotoxemia. Using the bacterial endotoxin sensitivity phenomenon (Shwartzman) Beeson[14] and Lee[15] demonstrated a marked increase in endotoxin sensitivity in animals after the reticuloendothelial system had been blocked by thorium dioxide (Thorotrast). Presumably, impaired reticuloendothelial function is followed by increased susceptibility to endotoxic shock. In idiopathic hemochromatosis, reticuloendothelial activity is greatly reduced by iron deposited within these specialized cells and, for this reason, such patients have increased risk from endotoxemia.

It seems unlikely that either ferritin release or endotoxemia actually initiate the shock process. In ferritin shock we would have to postulate a stage in idiopathic hemochromatosis when iron is spontaneously released into the circulation in sufficient quantity to disrupt completely blood-pressure regulation. In endotoxic shock, the disease would have to reach a stage when reticuloendothelial activity was so totally depressed that there was no detoxification of the endotoxins normally absorbed from the bowel. Because it is difficult to accept either of these postulates in idiopathic hemochromatosis, we must consider some primary mechanism that releases ferritin into the blood stream or finally disrupts an already damaged reticu-

loendothelial system. This initiating mechanism need not persist because, once established, untreated ferritin shock or endotoxemia will be self-perpetuating and progressive.

Although all the patients with hemochromatosis and profound shock have had severe abdominal pain, the role of this pain in the pathogenesis of shock has been ignored, even though in conscious subjects severe or prolonged pain can induce circulatory collapse. In patients with hemochromatosis, hepatic anoxia associated with shock could release ferritin into the circulation. In endotoxemia, the stress of anoxia on a reticuloendothelial system already depressed by iron deposition could induce a complete breakdown in function and thus promote shock. Therefore, whether ferritin or endotoxemia is responsible for the irreversible phase in hemochromatosis, the initiating mechanism is probably neurogenic shock secondary to the severe abdominal pain.

The surgeon always must be aware that idiopathic hemochromatosis may manifest itself in this way. However, certain common factors may assist him in reaching the correct diagnosis. Most of these patients are men in the 50- to 60-year age group. They may have a family history of hemochromatosis and may have increased pigmentation on exposed areas. Typically the skin is dark grey or slate coloured and only occasionally is truly bronzed. A flat plate of the abdomen may show increased density over the liver and spleen when compared with normal films.[16] When hemochromatosis is complicated by diabetes, the urine will contain sugar. The urine may also have iron-containing casts. Once the diagnosis has been entertained, serum iron and total plasma iron binding capacity should be estimated. Abnormal values are not absolutely diagnostic but, nevertheless, they substantiate the clinical diagnosis.

Diagnosis using oral cholecystography may be further complicated when the abdominal pain simulates acute cholecystitis as in Case 1. Uncompensated hemochromatosis interferes with hepatic uptake, conjugation and excretion of iopanoic acid (Telepaque) and, consequently, not enough contrast medium may reach the gallbladder to permit visualization;[17] hence, the erroneous clinical diagnosis of cholecystitis will appear to have been substantiated. In Case 1 gallbladder function was normal after the patient had repeated venesections, which suggests that some of the liver changes associated with this disease are reversible.

In the abdominal crisis in hemochromatosis, the first task is to manage the hypotensive state if this should develop. The blood pressure may fall for the first time shortly after the pain begins or it may fall only after the abdomen has been explored. Resuscitation in this progressive hypotension has been singularly ineffective and, in these circumstances, no patient has survived. Neither blood-volume expanders, nor hydrocortisone or Aramine are of demonstrated value. Because bacterial endotoxins or ferritin may contribute and because severe abdominal pain may initiate the shock, the surgeon should consider these when attempting to prevent or control progressive hypotension. Severe pain may be controlled either by pethidine or a morphine derivative. In our first case, pethidine quickly controlled the pain and at no stage in his illness did this patient have a fall in blood pressure. Antibiotics will protect against endotoxic shock and these should be given intravenously in large doses.[18] Because the endotoxin is produced in the bowel lumen, neomycin should be given orally and as enemas if the patient's general condition permits. To remove the circulating ferritin, the potent iron-chelating agent, desferrioxamine-B, should be given intravenously. By such methods the progressive hypotension of idiopathic hemochromatosis may perhaps be brought under control.

Summary

Abdominal pain was the presenting symptom in two patients with idiopathic hemochromatosis. While this mode of presentation is uncommon, it has great clinical importance. The various theories advanced to explain the abdominal pain are discussed. These patients may develop severe hypotension and the possible mechanisms responsible for this hypotension are considered. We have also outlined the man-

agement of patients with idiopathic hemochromatosis who present with severe abdominal pain, with or without hypotension.

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Résumé

Dans l'hémochromatose idiopathique, un trouble héréditaire du métabolisme du fer cause des dépôts excessifs de fer dans l'organisme. L'accumulation excessive de fer, sous forme de ferritine et d'hémosidérine, provoque la fibrose et des troubles fonctionnels des organes atteints. Chez certains malades, le seul symptôme présent est une douleur abdominale qui est parfois très vive et qui pose un problème de diagnostic différentiel avec les urgences chirurgicales courantes. Les deux malades que présentent les auteurs attirent l'attention sur l'hémochromatose primitive comme cause de douleur abdominale et illustrent certains problèmes diagnostiques et thérapeutiques qu'ont posés ces malades.

Chez deux malades, le seul symptôme présent était la douleur abdominale. Cette symptomatologie, quoique rare, revêt une grande importance clinique et les auteurs exposent les diverses théories invoquées pour expliquer cette douleur. Chez ces malades, peut se développer une hypotension sévère, dont les mécanismes possibles sont étudiés. Enfin, les auteurs proposent le traitement de ces urgences.

COMPARATIVE STUDY OF PROSTHETIC AND HOMOGRAFT VALVES IN THE GROWING CALF WITH REFERENCE TO AORTIC VALVE REPLACEMENT IN CHILDREN*

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AORTIC valve replacement in children presents special problems. A small ring may make valve replacement difficult. The effect of growth on the inserted valve and the effect of this valve on growth of the aortic area must also be considered. This paper presents our observations on the use of prosthetic and homograft aortic valves in the growing calf with particular attention to the influence of growth and how this might influence the use of such valves in children.

METHOD

The aortic valve was replaced in 2- to 5-week-old male Holstein-Friesian calves weighing between 100 and 140 lbs. The anesthetic technique and the care of the calves during and after operation were as described by other authors.[1-3] A median sternotomy incision was used. A rotating disc oxygenator primed with homologous blood drawn 48 hours previously was employed for cardiopulmonary bypass. The coronary arteries were perfused during the period of aortic occlusion. Prosthetic valves were inserted with interrupted horizontal mattress sutures of 00 Mersilene. Homograft valves sterilized in beta propriolactone were used either fresh or freeze-dried. They were secured in the sub-coronary position with two rows of sutures as described by Barratt-Boyes,[4] except that the donor aortic wall was not excised in the non-coronary sinus. In some calves, the non-coronary cusp alone was excised and replaced with a single homograft cusp including a section of homograft aortic wall. In one calf, the homograft aortic wall was not included and the cusp was sutured to a fringe of the recipient's cusp. Anticoagulants were necessary for long-term survival following insertion of a prosthetic valve.

Left heart catheterization and aortic root angiography, performed on a few

TABLE I.—CAUSE OF DEATH IN CALVES WITH PROSTHETIC AORTIC VALVES

Calf no.	*Weight (lbs.)*	*Aortic ring diameter (mm.)*	*Valve size*	*Duration of survival*	*Cause of death*
			Starr-Edwards valves		
36	151	26	8A	6 days	Coronary embolism
42	100	23	8A	7 "	Pneumonia
113	108	22	7AD	17 "	Hemorrhage; pneumonia
110	108	21	7AD	3 wks.	Valve thrombosis
118	116	22	9AD	3 "	Pyothorax
123	116	22	9AD	2 mos.	Valve separation
109	108	22	7AD	4 "	Valve thrombosis
			Gott-Daggett valves		
60	161	25	0-A	6 days	Valve thrombosis
58	136	26	0-A	4 wks.	Valve thrombosis
			Smelloff-Cutter valves		
116	113	23	M2	1 mo.	Hemorrhage
150	99	19	M1	4 mos.	Cardiac catheterization
127	99	23	M2	13 "	Aortic stenosis
148	95	20	M1	14 "	Aortic stenosis

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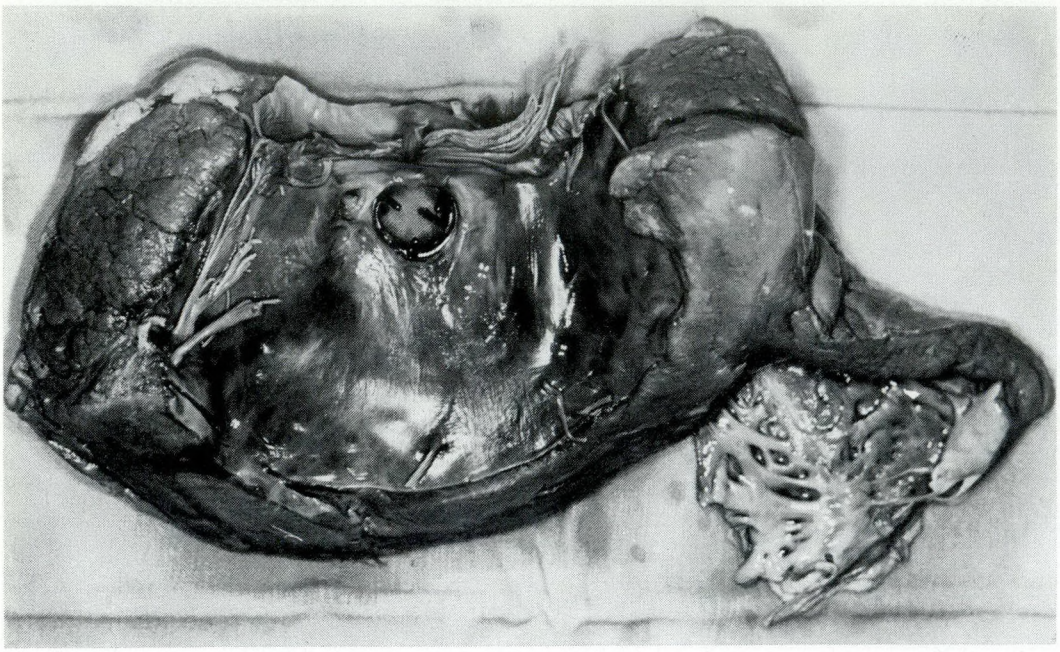

Fig. 1.—Section of the left ventricle of Calf 127, dying suddenly 13 months after the insertion of a Smelloff-Cutter valve, shows clearly the effective aortic stenosis with marked left ventricular hypertrophy and a relatively small valve orifice. The valve, adequate when the calf was small, became inadequate with growth.

animals three to four months after operation, contributed little additional information. Long-term survivors were observed until death or sacrifice, usually 8 to 12 months after operation. At that time the condition and function of the homograft valves were assessed with a pulse duplicating machine and by gross examination.

Results

Of the calves surviving 72 hours or more, 13 had had prosthetic valves inserted (Table I). Thrombosis, a major problem in those receiving prosthetic valves, was avoided by long-term anticoagulation therapy. Two calves survived 13 and 14 months respectively. They grew slowly and were relatively small at the time of their sudden death. Their hearts resembled those in patients with severe aortic stenosis. The left ventricle was markedly thickened and its outflow was limited to the diameter of the valve orifice (Fig. 1). There was no growth of the aortic root distal to the prosthetic valve ring.

Of the 11 calves who survived longer

TABLE II.—Growth of Aortic Ring in Calves With Homograft Aortic Valves

Calf no.	*Weight (lbs.)*	*Aortic ring internal diameter (mm.)*			*Duration of survival*	*Cause of death**
		Recipient	*Graft*	*At post mortem*		
146	109	22	20	20	5 days	Coronary obstruction
46	93	23	20	20	7 "	SBE
57	126	23	19	19	8 "	SBE
133	114	22	20	14	25 "	SBE + AS
52	103	22	20	15	6 wks.	SBE + AS
131	104	22	20	15	6 "	SBE + AS
80	148	25	21	12	2 mos.	SBE + AS
140	118	25	22	—	3 "	Sudden death
37	147	24	20	20	10 "	AI + AS
69	110	23	20	23	10 "	AI
141	114	23	21	24	12 "	AI + AS

*SBE = subacute bacterial endocarditis; AS = aortic stenosis; AI = aortic insufficiency.

TABLE III.—Growth of Aortic Ring in Calves With Homograft Valve Cusps

Calf no.	Weight (lbs.)	Aortic ring internal diameter (mm.)			Duration of survival	Cause of death
		Recipient	Graft	At post mortem		
74	108	24	24	24	4 days	Unknown
144	107	20	20	20	19 "	Pneumonia
65	99	21	20	21	5 wks.	Aortic insufficiency
104	107	19	19	25	6 mos.	Sacrificed
107	118	20	20	23	6 "	"
99	112	19	18	26	7 "	"
64	130	24	—	40	18 "	"
95	131	23	22	40	21 "	Aortic insufficiency

than 72 hours after homograft aortic valve replacement, six developed infection on the valve and died within a few months (Table II). Two calves survived 10 months and one 12 months. In all three the aortic valves were incompetent at the time of death. The diameter of the valve ring was unchanged in one calf and increased by only 3 mm. in the other two. This slight increase occurred in the region of the right and left coronary cusps where only a small strip of homograft aortic wall had been retained. There was no growth in the region of the non-coronary cusp where more homograft aortic wall had been inserted.

Eight calves receiving homograft non-coronary valve cusps survived more than 72 hours and five were observed for 6 to 21 months (Table III). At death or sacrifice, all had some insufficiency in the region of the homograft cusp. The aortic valve ring had grown in the region of the recipient's own coronary leaflets. There was no growth of the homograft non-coronary valve cusp or of the aortic wall to which it was sutured (Fig. 2). The calf in which the cusp was transplanted without a rim of homograft aortic wall had some growth of the recipient aortic wall but no growth of the cusp itself, and the valve was incompetent (Fig. 3).

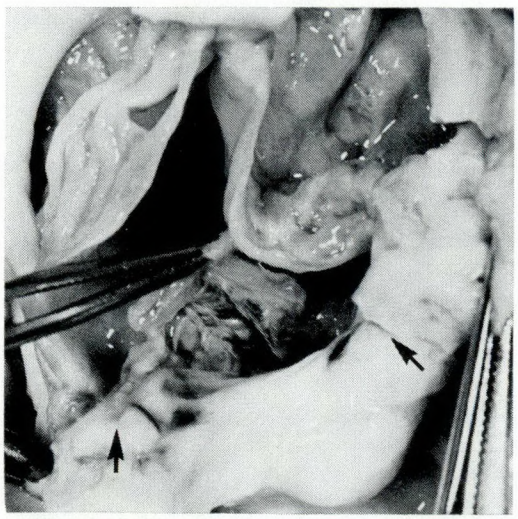

Fig. 2.—Aortic valve of Calf 107 at sacrifice six months after replacement of the non-coronary cusp with a homograft cusp and its adjacent aortic wall. The cusp (between arrows) is small, thin, friable and insufficient. The donor aortic wall has been incorporated into the recipient aortic wall with thick scar formation. This portion of the aortic ring has not grown in comparison with the area about the two normal coronary cusps.

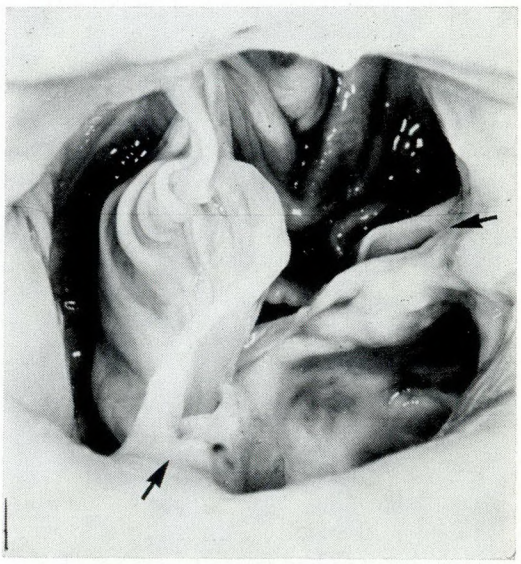

Fig. 3.—Aortic valve of Calf 95 which died 21 months after almost complete replacement of the non-coronary cusp with a homograft aortic cusp. The donor cusp alone, without aortic wall, was sutured to a short fringe of the recipient's cusp. The cusp is now thickened, small and moderately insufficient. Although it has not grown appreciably there has been relatively little interference with aortic ring growth compared to that shown in Fig. 2.

Discussion

For some years aortic valve replacement has been accepted as a therapeutic procedure. The relative superiority of prosthetic valve versus homograft valve has often been discussed, particularly with reference to function and durability. In comparing these factors the present investigation does not repeat the work of others but rather considers one other factor specific to children, the effect of growth.

We found that valve replacement in calves, whether homograft or prosthetic, interfered with growth of the aortic valve ring. There was no growth with prosthetic valves, and only partial growth with homograft valves and this was related to the presence of homograft aortic wall. Where only a thin rim of the donor aortic wall was implanted, such as adjacent to the coronary cusps, there was slight growth of the aortic valve ring, while in the region of the non-coronary cusp where the donor aortic wall was not trimmed between the commissures, there was no significant growth. The reaction of the donor aortic wall has been noted by other authors.[5, 6] The pathological changes in aortic valve homografts in the human have been well described by Hudson[7] and Smith.[8] We sterilized the valves in beta propriolactone and found no appreciable difference in the results with fresh or freeze-dried valves. Other methods of preservation were not tested.

In an older child who has had enough aortic incompetence to create an aortic valve ring of adult proportions, the decision to use a homograft or a prosthetic valve is no different than in the adult patient. The choice depends on the experience of the surgeon who, with due regard to the performance record of the two valves, will balance the greater availability and easier insertion of the prosthetic valve against the benefit of avoiding anticoagulants when the homograft valve is used.

In a young child with aortic insufficiency and a relatively large aortic valve ring, it should be possible technically to insert either a prosthetic or a homograft valve. If the valve ring will accept an adult-sized prosthetic valve, this may be preferable to a homograft valve because further growth of the patient's valve ring might otherwise lead to insufficiency of the homograft valve.

If the valve ring is not large enough to admit an adult prosthetic valve, the homograft valve offers some advantages. It provides a larger flow area in relation to its external diameter and thus allows for the child's growth and his need for increased cardiac output. In addition, if only a small amount of homograft aortic wall is left on the homograft valve, the aortic ring may grow somewhat which, while leading to recurrent aortic insufficiency, will also permit the subsequent insertion of a larger valve. These advantages must be weighed against the technical difficulties of homograft valve insertion and the problem of finding a homograft of proper size.

On two occasions, we have been forced to consider valve replacement in a child with a small aortic valve ring. Both were children with previously treated aortic stenosis and an essentially bicuspid aortic valve. The stenosis could not be relieved adequately without producing serious aortic insufficiency and the aortic valve ring was too small to accept any prosthetic valve. Nothing further could be done for these children and we wonder whether a small aortic valve ring might be stimulated to enlarge by deliberately producing mild aortic insufficiency at the primary aortic valvotomy. Failing this, we are attempting to find some satisfactory technique for safely enlarging the aortic ring.

Although Barnes, Mohri and Merendino[9] got satisfactory results by implanting single homograft aortic valve cusps into adult dogs, this seems unsatisfactory for the growing child. Not only is it technically difficult to insert the cusp and have it function adequately but since it fails to grow, insufficiency results.

Summary

Thirty-two young calves surviving 72 hours or longer following replacement of the aortic valve with a prosthetic or a homograft valve, or replacement of a single aortic valve cusp with a homograft cusp were examined at death or sacrifice

to study the relationship between the growth of the calf and the type of valve used. We found that the prosthetic valves produced severe and limiting aortic stenosis as the calves grew. Growth of the aortic ring area was definitely reduced wherever homograft aortic wall was inserted. When a wide section of homograft aorta was used, as in the non-coronary sinus area, growth of the ring ceased.

In a child with an aortic valve ring of adult size, growth does not affect the choice of valve to be used. When the aortic ring is small, however, one must consider the limiting effect of the valve on growth of the ring and, if a homograft valve is used, the possible effect of growth on the function of the valve.

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Résumé

En vue de déterminer l'effet qu'exerce la croissance sur la fonction d'une valve de remplacement et de choisir à bon escient le type de valve à utiliser chez l'enfant, nous avons étudié chez le jeune veau le fonctionnement de la valvule aortique remplacée soit par une prothèse, soit par une homogreffe.

Les valves de prothèse arrêtent la croissance dans la zone de la valvule et peuvent être employées avantageusement si l'anneau de la valvule aortique est assez grand pour recevoir une grande valve.

Les valves réaliséees par homogreffe inhibent la croissance dans une mesure proportionnelle à la quantité de paroi du donneur qui y est fixée. Si on ne transplante qu'un mince anneau de la paroi aortique, la valve du receveur va croître dans une certaine mesure et entraîner à la longue une insuffisance valvulaire. Cette croissance relative peut être nécessaire chez un enfant dont l'anneau valvulaire est de petite dimension: elle prévient la sténose et permet d'insérer ultérieurement une valve plus grande. Ceci constitue un net avantage, malgré les problèmes que posent l'obtention et l'insertion de petites homogreffes valvulaires.

MULTIFOCAL EPILEPSY

Treatment of multifocal epilepsy requires accurate anatomical localization of the foci. Of 1000 patients with traumatic epilepsy studied in the Institute of Neurosurgery, Leningrad, 300 underwent operation for a single epileptic focus. Of 17 patients who were operated on for multifocal epilepsy, 15 had two foci and two had three. In all, the foci were in one hemisphere, most frequently in the left. Mostly they were localized in the sensory zone of the temporal lobe.

Adhering to the principle of "physiological" permissibility, the epileptogenic foci were removed by stages. Subcortical epileptic foci are small and in their removal only a few millimetres of brain tissue are destroyed.

The authors regard the dominant epileptogenic focus not only as the permissive mechanism of seizures, but also as a focus that disorganizes the integrative functions of the cerebral cortex and the functions of the various structures of the brain. From this point of view removal of the epileptogenic focus can be regarded to some extent as treating the cause. The success of such surgery is largely determined by proper screening of patients and application of modern methods and techniques. —Ugryumov, V. M. *et al.*: Refinements of indications and surgical approach in treatment of multifocal epilepsy, *Voprosyi Neirokhirurgii*, **3:** 4, 1969.

ARTIFICIAL GILL (CELLOPHANE-MEMBRANE COIL DIALYZER) IN RESPIRATORY INSUFFICIENCY*

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UNTIL recently most oxygenators were developed exclusively for extracorporeal perfusions during cardiac surgery, and because of their efficiency, oxygenators with a direct blood-gas interface were usually employed. As long as the perfusions were short, the deleterious effects of these oxygenators were, to a certain extent, acceptable. On the other hand, long perfusions damaged the blood,[1, 2] denatured the proteins,[3, 4] caused pulmonary changes[5] and a higher mortality rate.[6, 7] Since the lungs were one of the main targets for these lesions, gas-exchangers of this type could obviously not be used for the prolonged treatment of patients suffering from various types of pulmonary insufficiency. Membrane oxygenators, on the other hand, although relatively inefficient, are less traumatic.[8-10] Since even pulmonary "cripples" can carry out some respiratory exchange, the need was not for a highly efficient oxygenator but for a safe one that could be used for long periods.

Carbon dioxide and oxygen diffuse better through Teflon and silicone rubber membranes than through cellophane, and for this reason these materials have been used more frequently for the construction of membrane lungs.[11, 12] Cellophane, however, because it is wettable, is theoretically more desirable[13] and can be used as a hemodialyzer, oxygenator and carbon dioxide extractor. Firme *et al.*[14] suggested its use and Chamberlain[15] employed it to manage infants suffering from the respiratory distress syndrome.

The purpose of the following investigation was to develop a relatively simple method of extracorporeal oxygenation that would not require extensive surgery and could be used for prolonged perfusions. We wished also to evaluate the oxygenating and carbon-dioxide extraction capabilities of the Kolf coil cellophane membrane* commonly used in hemodialysis.

MATERIALS AND METHODS

Small mongrel dogs of various ages and weights (between 3 kg. and 11 kg.) were anesthetized with sodium pentobarbital (25 mg./kg.) and intubated with a leakproof endotracheal catheter. The first five animals were used to develop and standardize the technique and were perfused only for one to two hours. Then Group 1, six animals, was perfused for four hours. Group 2, another six animals, was perfused for six hours.

Description of the Apparatus

The cellophane-membrane Kolf coil surrounded by a pressure cuff was placed in the canister of a hemodializing unit† which had been modified by inserting the end of an oxygen tube into a disperser (or diffuser) between the recirculating pump and the artificial kidney canister (Fig. 1). The oxygen (10 to 15 l./min.) was thus bubbled

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*Ultra Flo 145 dialyzer, Travenol Laboratories, Inc., Morton Grove, Ill.

†Travenol 100-l. tank hemodialyzing unit and Travenol kidney roller pump, Morton Grove, Ill.

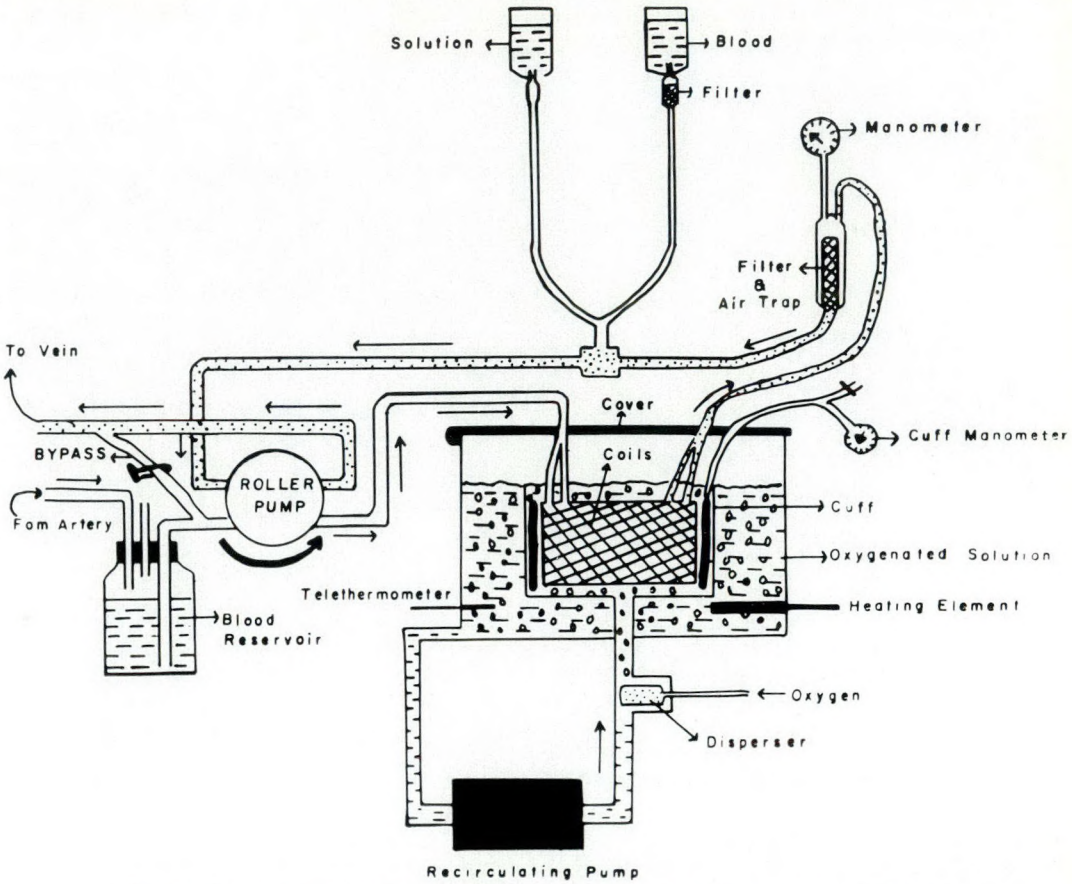

Fig. 1.—Arteriovenous perfusion with the cellophane-membrane coil oxygenator.

into the dialyzing fluid* which became saturated (600 to 800 mm. Hg).

Because we evaluated this "artificial gill" in dogs with an arteriovenous bypass, blood from the artery was collected in the reservoir; from there it was pumped into the cellophane-membrane coil where the blood, coming in contact with the oxygenated fluid, became saturated and gave up some of its carbon dioxide. The cuff around the coils was inflated to 250 mm. Hg to obtain a thin blood film. The blood was then passed into a blood filter and air trap connected to a manometer. The fluid lost by dialysis caused a drop in the pressure of this circuit which was recorded by the manometer. In order to compensate for this fluid loss, either blood or an electrolyte solution was added at a rate adjusted to maintain a constant pressure in the circuit. From the filter, the blood was returned to the pump and injected into the vein. The temperature of the bathing fluid was maintained around 38 or 39° C. Blood flows per minute equal to one-third of the blood volume were used for the arteriovenous bypass (Fig. 1).

The oxygenator dialyzer was primed with heparinized (25 mg./500 ml.), typed, and cross-matched blood (400 to 500 ml.) in order to decrease the risk of hemolysis which killed two animals during the preliminary study.

Methods of Perfusion

The dog was placed on a scale to observe changes in blood volumes. Its temperature was maintained at normal levels with a heating blanket. The brachial vessels were cannulated and connected to pressure transducers; the transducers were

*Forty litres of Travenol dialysate made from the dialysate salt concentrate-100, Travenol Laboratories Inc., Morton Grove, Ill.

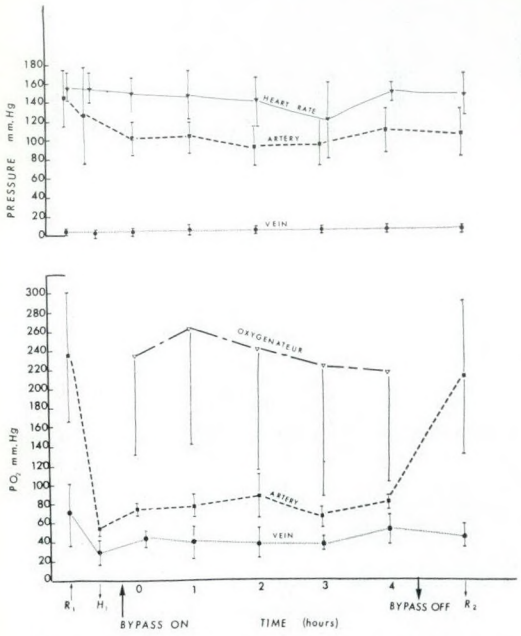

Fig. 2.—Pressures and Po_2 tensions during four hours of arteriovenous perfusion with the cellophane-membrane coil (mean ± SD).

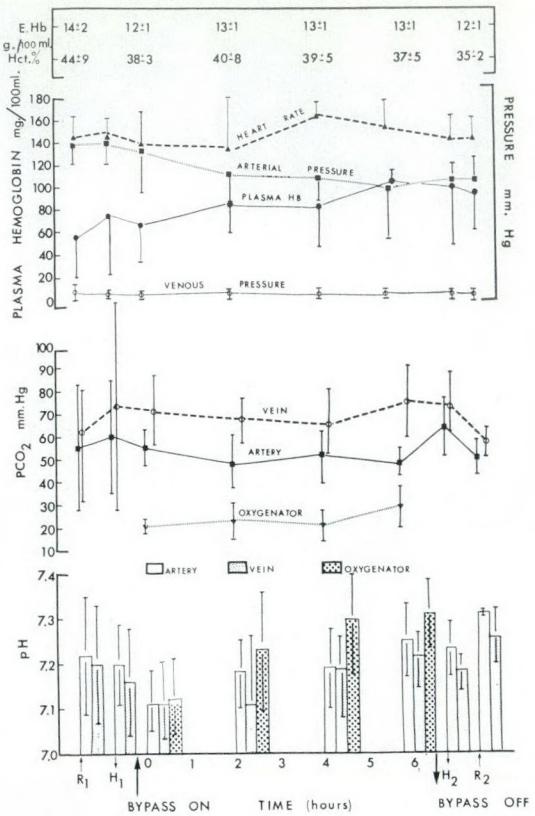

Fig. 3.—Hematologic and biochemical data obtained during four hours of arteriovenous perfusion with the cellophane-membrane coil (mean ± SD).

then connected to a radiometer* modified to give Po_2, Pco_2 and pH readings in a semi-continuous manner.

The left femoral vessels were then dissected, the animal was heparinized (2 mg./kg. followed by 1 mg./kg. every 1½ hours) and the largest possible cannulas were used to connect the vessels to the extracorporeal system. The endotracheal tube was connected to the closed circuit of an anesthesia machine and a gas mixture needed. The oxygen content of the gas mixture was then reduced to lower the arterial oxygen tension to about 50 mm. Hg. After approximately 10 minutes of hypoxia, the perfusion was started and maintained for four to six hours. The venous hemoglobin was measured before, during and after the perfusion. The electrocardiogram (ECG), electroencephalogram (EEG), arterial and venous pressures were continuously monitored on a multi-

TABLE I.—Total Plasma CO_2, Base Excess and Standard Bicarbonates in Group 1 (Mean ± S D)

*Time** (hrs.)	*Total plasma CO_2 (mEq./l.)* Artery	Vein	Oxygenator	*Base excess (mEq./l.)* Artery	Vein	Oxygenator	*Standard bicarbonate (mEq./l.)* Artery	Vein	Oxygenator
R_1	20.4 ± 6.9	22.4 ± 6.9	—	−8.5 ±3.01	− 7.8 ± 3.2	—	18 ± 2	18.4 ± 2.4	—
H_1	17.7 ± 7.6	15.9 ± 6.5	—	−9.7 ± 4.8	−12.6 ± 5.4	—	21.1 ±11.2	15 ± 3.7	—
0	23.1 ± 9.1	30.1 ±15.9	12.6 ±6.4	−6.3 ± 9.2	− 1.9 ±16.3	−14.3 ±5.6	19.3 ± 6	23.8 ±12.9	14.1 ±3.3
1	16.7 ± 7.4	16.6 ± 8.3	9.6 ±3.8	−9.4 ± 6.4	− 9.3 ± 7	−16.8 ±4.7	15.5 ± 4	15.5 ± 3.8	12.7 ±3.8
2	18.4 ± 9	22.2 ± 8	9.0 ±1.8	−9.8 ± 8.3	− 9.3 ± 9.5	−17.2 ±2.7	17.3 ±6.4	18 ± 6.3	11.7 ±1.5
3	16.0 ± 8.1	29.2 ± 7.5	7.9 ±4.9	−7	−12.5 ±13.4	−20.7 ±3.8	14.8 ±9.1	21.7	10.5 ±1.4
4	22.4 ±10.2	25.7 ± 9.2	12.3 ±2.4	−4.7 ± 6.3	− 3.1 ± 6.6	−13.6 ±4.7	20.7 ±4.9	22.1 ± 4.9	14.4 ±2.9
R_2	26.1 ±11.4	20.5 ±15.5	—	−6.3 ±10.8	− 0.7 ± 9.8	—	19.9 ±8.1	17.3 ± 8.6	—

*R_1 and R_2 = animals on respirator breathing a gas mixture rich in oxygen. H_1 = hypoxic animals—breathing a gas mixture poor in oxygen.

(nitrous oxide and oxygen) rich in oxygen was given initially. All respiratory movements were then stopped with an intravenous injection of tubocurarine chloride (Tubarine) which was repeated when

*Bach-Simpson Limited, London, Ont.

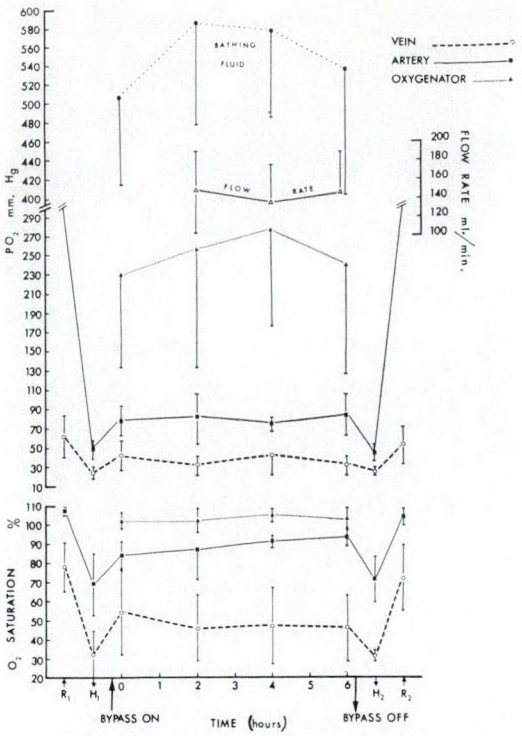

Fig. 4.—Physiologic, hematologic and biochemical values obtained during six hours of arteriovenous perfusion with the cellophane-membrane lung (mean ± SD).

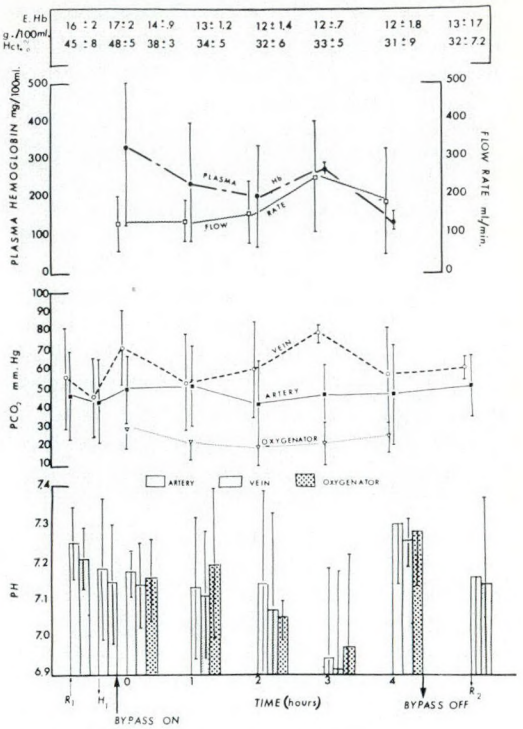

Fig. 5.—Flow rate, P_{O_2} and oxygen saturation during six hours of arteriovenous perfusion with the membrane lung (mean ± SD).

channel oscilloscope, while the P_{O_2}, P_{CO_2} and pH were measured from the artery, the vein and the oxygenator by the Astrup technique.[16] The base deficit, standard and actual bicarbonate levels were calculated from the Siggaard-Andersen curve before and at the end of the perfusion with radioiodinated (^{131}I) human albumin (RISA) and a gamma scintillation counter.* These parameters were measured (1) before the bypass, while the animal was breathing the gas mixture in oxygen (R_1); (2) during hypoxia (H_1); (3) at intervals during perfusion; (4) after stoppage of the bypass, with the animal still breathing the hypoxic mixture (H_2); and (5) with the animal on the respirator breathing pure oxygen (R_2).

TABLE II.—Total Plasma CO_2, Base Excess and Standard Bicarbonates in Group 2 (Mean ± S D)

Time* (hrs.)	Total plasma CO_2 (mEq./l.) Artery	Vein	Oxygenator	Base excess (mEq./l.) Artery	Vein	Oxygenator	Standard bicarbonate (mEq./l.) Artery	Vein	Oxygenator
R_1	22.6 ±9.2	22.2 ± 7.3	—	− 7.53 ±7.3	−6.6 ± 6.7	—	20.2 ±6.7	19.4 ± 4.7	—
H_1	21.4 ±9.2	27.9 ±18.3	—	− 8.7 ±9.9	−3.7 ±12.6	—	17 ±5	22.1 ±10.1	—
0	19.3 ±2.7	24.2 ± 5.7	8.4 ±1.4	−11.7 ±3.2	−7.5 ± 5.4	−21.6 ±4	15.5 ±2.2	18.4 ± 4	9.8 ±2.2
2	16.7 ±5.7	27.5 ± 3.6	10.1 ±2.8	−10.7 ±5.6	−2.5 ± 4	−15.3 ±3.7	16.4 ±3.7	22.2 ± 3.1	12.4 ±2.9
4	21.2 ±7.7	25.8 ± 8.8	11.7 ±2.1	− 8.4 ±8.3	−4.3 ± 9.8	−14.6 ±5.7	18.5 ±5.7	21.4 ± 7.5	13.8 ±3.5
6	21.3 ±2	32.7 ±11.7	14.9 ±3.7	− 5.7 ±4.1	2.1 ±11.1	−10.7 ±3.2	19.7 ±3.2	25.9 ± 8.8	16.2 ±2.3
H_2	28.7 ±7.8	28.9 ±10.7	—	0.11 ±8.8	−2.7 ± 9.2	—	23.6 ±9.2	21.4 ± 8.7	—
R_2	25 ±5.6	27 ± 9	—	− .16 ±6.1	−2.25 ± 8.8	—	23.3 ±3.8	22.8 ± 7.5	—

*R_1 and R_2 = animals on respirator breathing a gas mixture rich in oxygen. H_1 and H_2 = hypoxic animals—breathing a gas mixture low in oxygen.

nomograms. The oxygen saturation was determined from a cuvette with a Waters oximeter.* The plasma hemoglobin was determined by spectrophotometric analysis. Blood volume determination was made

*Waters oximeter XP-350, Waters Company, Rochester, Minn.

*Nuclear-Chicago Corporation, Des Plaines, Ill.

Postmortem and histopathologic studies were performed on all animals that died and on all that survived, one to three weeks after operation.

Results

The results in the Group 1 are shown in Figs. 2 and 3 and Table I; those in Group 2 are shown in Figs. 4 and 5 and Table II.

Except for occasional minor changes in rhythm, the ECG and EEG were considered to be within normal limits. White and red blood cell counts were made a week after operation in three dogs in Group 1 and five in Group 2. In general they showed a small, but definite, drop in the erythrocyte count (Table III).

Three dogs in Group 1 died within 24 hours after operation. At autopsy, one had a huge mediastinal hematoma and blood in both thoracic cavities, probably due to traumatization of the vena cava during cannulation of the heparinized animal. Another had severe cerebral congestion, but both lungs were normal. The third animal had some pulmonary congestion and edema of both lungs probably due to overloading. Of the dogs that were killed a week later, one showed diffuse atelectatic areas (Fig. 6) in both lungs while the lungs of the other animals were essentially normal.

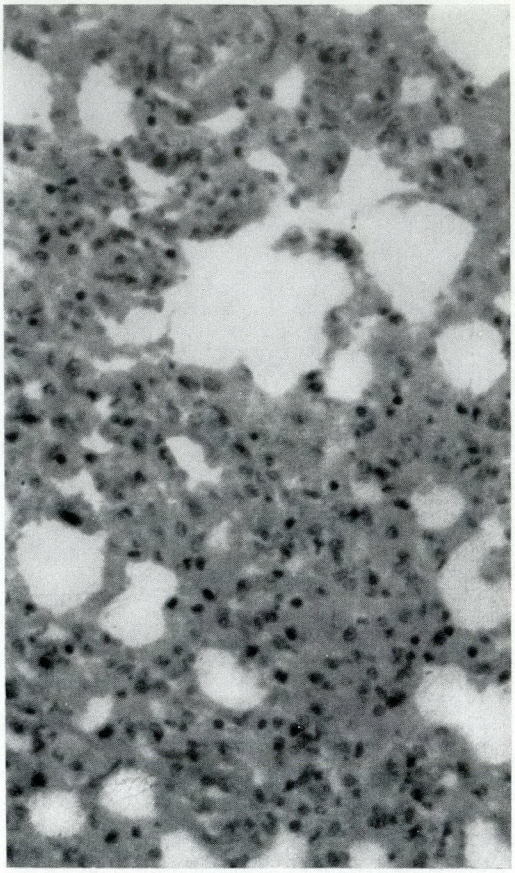

Fig. 6.—Section of the lung of a dog perfused for six hours showing multiple areas of diffuse atelectasis (hemalum-phloxine-saffron stain, original magnification × 250).

TABLE III.—Hematologic Data Before and One Week After Perfusion (Mean ± S D)

	Hemoglobin (g./100 ml.)	*Hematocrit (ml./100 ml.)*	*Red blood cell count (10^6/mm.^{3})*	*Total leukocyte count (10^3/mm.^{3})*
Before perfusion	13 ± 1.4	43 ± 2.3	5 ± 1	6 ± 1
One week after perfusion	9.4 ± 1.4	28.5 ± 4.6	3 ± .6	3 ± 2

In Group 2, dogs perfused for six hours, there was one postoperative death and postmortem studies revealed only mild pulmonary congestion. Another dog whose general condition was deteriorating was sacrificed two days after operation; this animal had congestion of both lower pulmonary lobes and cardiac dilatation.

Discussion

Although the oxygenating capacity of cellophane membranes is somewhat limited at high flow rates, it appears that in small hypoxic animals and with the low flow rates used, these membranes will give a worthwhile increase in arterial oxygen tension. Carbon dioxide extraction has also been acceptable, probably because of the good diffusion of this gas in a liquid medium.[9, 17]

The plasma hemoglobin, which in the heparinized animals of the second group averaged 58 mg./100 ml., rose at the beginning of the perfusion because of minor

incompatibilities in the priming blood and trauma from the pump. Thereafter there was only slight variation in the level which remained always within acceptable limits. It should be noted, however, that the post-perfusion anemia would suggest an increased fragility of the red blood cells. Whether this was caused by the pump or the oxygenator needs to be investigated further.

In three dogs there was a significant reduction in the blood return during the bypass and consequently the blood flow had to be reduced. Part of this reduction could be explained on the basis of blood loss. However, it might have been due to pooling and sequestration of the blood in the vascular bed.[18-20]

The cardiac dilatation found in one dog and the pulmonary edema noted in four may have been due either to cardiac failure or to circulatory overloading. On the other hand, Rashkind *et al.*[21] did not observe any increase in cardiac work following arteriovenous perfusions with a bubble oxygenator in hypoxic puppies.

In addition to the extracorporeal respiratory gas exchanges obtained with this technique, other benefits are: (1) control of body temperature by varying the temperature of the bathing fluid; (2) regulation of acid-base balance; (3) maintenance of blood electrolyte homeostasis; and (4) availability of another route for nutrition.

Summary and Conclusions

An artificial gill made of cellophane-membrane coils was evaluated in the dog during arteriovenous perfusions for four to six hours. We used a modified commercial kidney unit and bubbled oxygen into the dialyzing fluid until saturation was reached. In small dogs satisfactory oxygenation of the blood was obtained with flows of 160 ml. Carbon dioxide extraction was also good. Very little hemolysis occurred with this technique. Slight anemia was noted one week after operation. At autopsy the main lesions were: diffuse patches of pulmonary atelectasis, congestion and edema, and cerebral congestion. These were probably due to overloading of the circulation and were relatively mild when compared to the severe changes noted with current oxygenators that have a direct blood-gas interface.[22-26] Most of the animals killed from one to three weeks after operation showed essentially normal organs.

This technique could also be used to control the temperature, the electrolyte and acid-base balance and to provide a route for the nutrition of the experimental animal or the human subject.

The authors would like to thank Mrs. L. Du Berger for her technical assistance.

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RÉSUMÉ

Pour traiter l'insuffisance respiratoire, les médecins préféreraient un oxygénateur qui pourrait être employé durant de longues périodes sans altérer le sang ni léser d'autres organes, même au dépens de la perte d'une certaine efficacité. Nous avons donc évalué le pouvoir d'échange gazeux d'un serpentin à membrane cellophanique chez 12 chiens hypoxiques au cours de perfusions artérioveineuses d'une durée de quatre à six heures. Nous avons utilisé à cette fin un rein artificiel modifié dans lequel le liquide de dialyse était saturé de bulles d'oxygène par une ouverture pratiquée dans le réservoir. Au débit moyen de 160 ml/mn nous avons porté la Po_2 de sa moyenne de 50 mm Hg qu'elle était durant la période d'hypoxie à environ 80 mm Hg et avons gardé l'hémolyse à moins de 250 mg/100 ml. L'élimination du gaz carbonique est demeurée en dessous du niveau antérieur à la perfusion. Lors de l'examen nécropsique, quatre chiens avaient de l'atélectasie, de la congestion et de l'œdème pulmonaire et une autre de la congestion cérébrale: ces modifications étaient probablement la conséquence d'une surcharge. Outre son indication dans les fonctions respiratoires, cet appareil peut servir à régler la température, à assurer la régulation de l'équilibre acide-base à maintenir l'homéostase des électrolytes du sang et pourrait servir de voie d'accès pour alimenter un malade.

SUBARACHNOID HEMORRHAGE AND CEREBROARTERIAL SPASM

Arterial spasm, one of the most serious complications of ruptured cerebral aneurysm, leads frequently to ischemia, edema and softening of the brain. The authors studied the spread of subarachnoid hemorrhage along the perivascular spaces and attempted to produce arterial spasm experimentally. The stress and rupture of the connective tissue suspending the arteries in the perivascular channels and irritation of the nerve elements in the arterial walls apparently play a substantial role in producing arterial spasm.

Injection of washed erythrocytes into the channels did not produce any arterial spasm. However, when blood clots were formed in the perivascular channels or when serotonin was introduced into them, arterial spasm was promptly produced.

The authors believe that late arterial spasm after subarachnoid hemorrhage may be explained by the delay of serotonin transport to the area of hemorrhage because of obstruction to intracerebral circulation. Bleeding into the cerebrospinal fluid leads to the formation of solid blood clots which block the intraventricular circulation and prevent serotonin from reaching the affected area and exerting its arteriospastic effect. However, after three to four days these thrombi break down, spinal fluid circulation is restored and serotonin arrives at the site of the hemorrhage and causes arterial spasm.—Arutyunov, A. I., Baron, M. A. and Maiorova, N A.: Study of subarachnoid hemorrhage with regard to pathogenesis of cerebroarterial spasms, *Voprosyi Neirokhirurgii*, **5:** 4, 1969.

AN AUXILIARY LUNG*

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We have constructed a tubular membrane oxygenator for use in extracorporeal circulation in infants.[1] It might also be used as an auxiliary lung in the treatment of temporary pulmonary insufficiency, as in neonatal respiratory distress syndrome or inflammatory pulmonary diseases of older children and adults, or of chronic pulmonary insufficiency in patients with emphysema.

In a membrane oxygenator the blood is separated from the oxygen by a gas permeable membrane. In our design, two sizes of silicone rubber tubing are used instead of conventional sheet membranes. Many fine tubes are placed inside a large piece of tubing.

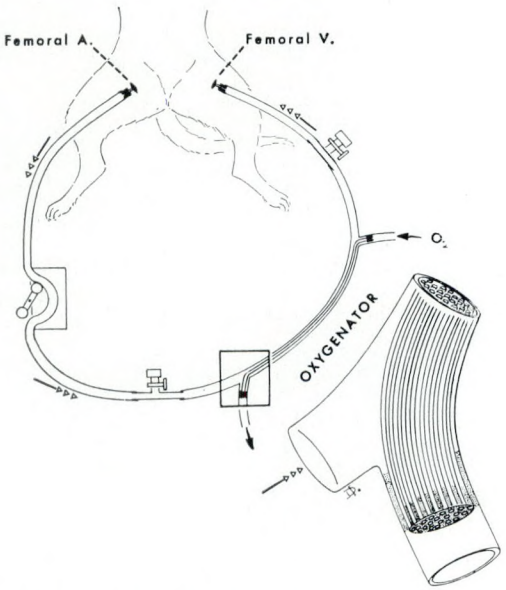

Fig. 1.—Partial bypass from artery to vein. Blood samples are drawn through stopcocks on either side of the oxygenator. Diagram of the tubular membrane oxygenator.

Material and Methods

Oxygenator

Silicone rubber tubing* was used for both large and fine tubing: 68 pieces of fine tubing with an inside diameter of 0.020 inches and an outside diameter of 0.037 inches were passed through a larger outside tube with an inside diameter of 0.375 inches and an outside diameter of 0.5 inches resulting in a total effective length of 816 inches of fine tubing.

Oxygen is blown through the fine tubes and blood flows through the large tube, around and between them. The gas exchange takes place through the wall of the fine tubing (Fig. 1).

To improve the irregular flow pattern of the blood in the oxygenator and thereby to increase the oxygen transfer rate, the oxygenator is rhythmically compressed.

Experimental Design

Each of 13 dogs was subjected to a two-phase experiment. In Phase 1 the dog breathed a lethal hypoxic mixture but was kept alive by introducing the oxygenator into the circulation. In Phase 2, carried out two to three weeks later, no oxygenator was used and the dog died breathing the same gas mixture.

To exclude any beneficial effects of the arteriovenous bypass *per se*, partial bypass was established in two dogs during Phase 2 as in Phase 1, but no oxygen was added to the oxygenator. Both dogs died.

In five dogs no attempt was made to control the body temperature. In two experiments, the rectal temperature was measured and found to drop 2° C. during the procedure. The results, therefore, were unreliable and, because of this finding, the next six dogs were placed on a heating blanket thus preventing the fall in body temperature. In this paper, we report the results obtained in these six dogs.

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*Silastic, Dow Corning Corporation, Midland, Mich.

Experimental Procedure

To prevent a fall in body temperature, which might lead to lower oxygen consumption due to hypothermia, the dog was placed on a heating blanket which was then folded around him, leaving the ventral surface exposed.

Anesthesia was induced with intravenous thiopental (Pentothal) and maintained with nitrous oxide and halothane via an endotracheal tube using an Air Shields constant volume respirator. The dogs were heparinized with 2 mg./kg. heparin supplemented every hour with 10 mg., both given intravenously.

For the partial bypass, a femoral artery and the femoral vein in the opposite leg were cannulated (Fig. 1). The oxygenator and the tubing were primed with normal saline solution. The resistance in the oxygenator was low enough to allow flow from artery to vein, but the flow was variable so an occluding roller pump was used to keep flow constant at 50 ml./min.

The amount of oxygen in the nitrous oxide mixture was decreased over a 30-minute period to 10%, resulting in an arterial oxygen tension between 20 and 30 mm. Hg—the range encountered in severe respiratory insufficiency in humans. The animals were maintained on this mixture of gases for 2½ hours. During the whole procedure (three hours) the auxiliary lung functioned.

Blood samples were drawn simultaneously with disposable syringes through stopcocks on either side of the oxygenator and labelled E (entering oxygenator) and L (leaving oxygenator).

The pH, Po_2 and Pco_2 in the samples were determined without delay on an Instrumentation Laboratory physiological gas analyzer and the hemoglobin was determined with a Spencer hemoglobinometer. The base excess was calculated with a Severinghaus blood-gas calculator. The oxygen content was calculated from the Po_2 and hemoglobin measurements. These determinations were repeated every 15 minutes until the end of the experiment. Free hemoglobin was measured every hour by the method of Hunter, Grove-Rasmussen and Soutter.[2]

TABLE I.—Blood Gases, Base Deficit and Plasma Hemoglobin in One Experimental Animal*

Dog 391. Weight 33 lbs.		*April 25, 1969. Phase 1*											*May 9, 1969. Phase 2*							
Time		*1100*	*1115*	*1130*	*1145*	*1200*	*1215*	*1230*	*1245*	*1300*	*1315*	*1330*	*1345*	*1400*	*1045*	*1100*	*1105*	*1115*	*1125*	*1135*	*1145*	*1155*
Hemoglobin (g./100 ml.)		10.5	12.5	12.0	11.5	12.5	13.5	11.0	13.0	15.8	14.0	14.4	15.0	13.5	10.5	—	—	—	11.8	—	—	13.5
pH	E	7.4	7.4	7.4	7.4	7.4	7.5	7.5	7.4	7.4	7.5	7.5	7.4	7.5	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.3
	L		7.4	7.4	7.4	7.4	7.5	7.5	7.4	7.4	7.4	7.4	7.4	7.5								
Po_2 (m.m. Hg)	E	45	58	39	36	35	15	13	30	29	30	30	60	67	134	46	42	37	21	17	19	16
	L		215	165	190	300	27	33	55	47	45	44	200	260								
Pco_2 (mm. Hg)	E	35	38	30	25	26	23	19	34	29	25	23	30	21	33	31	32	23	25	26	24	28
	L		30	30	26	31	27	20	28	29	25	23	30	21								
Hemoglobin saturation (%)	E	81	93	80	69	70	23	17	58	56	61	62	91	95	96	83	77	73	36	27	30	18
	L		100	100	100	100	55	67	89	84	82	82	100	100								
Oxygen content (ml./100 ml.)	E	11.4	15.6	12.9	10.7	11.7	4.1	2.5	10.1	11.8	11.5	11.9	18.4	17.2	13.2	11.1	10.3	11.5	5.7	4.2	5.3	2.8
	L		16.8	16.1	15.4	16.8	9.9	9.9	15.5	17.7	15.3	15.7	20.1	18.1								
Base excess (mEq./L)		−3	−2	−4	−9	−6	−8	−9	−1	−5	−7	−8	−5	−10	−6	−4.5	−4.5	−8	−7	−8	−9	−12
Plasma hemoglobin (mg./100 ml.)		36				52				62				78								

*During the experimental run, two samples of blood were studied: E = blood entering oxygenator, and L = blood leaving oxygenator. Arterial blood was studied during the control run.

At the end of Phase 1, the cannulas were removed, the blood vessels ligated and the incisions closed. No heparin antagonist was given.

Two to three weeks later, when the hemoglobin had returned to the pre-experimental level, the second phase of the experiment was carried out. Each dog was anesthetized as before and an arterial cannula was inserted into a brachial artery. The respiratory gas was then altered gradually, duplicating as nearly as possible the events of Phase 1 until the dog was breathing the hypoxic mixture. As in Phase 1, the pH, Po_2, Pco_2 and hemoglobin levels were determined on arterial blood every 15 minutes until the animal died.

Results

The complete data obtained in one experiment are presented in Table I as a representative example. The changes in the acid-base balance, a progressive increase of the base deficit, were similar in both phases. The difference in the oxygen content between the blood leaving the oxygenator and the blood entering the oxygenator was 3.2 to 7.4 vol. %, excluding two samples with saturated hemoglobin.

The oxygen content of the blood entering and leaving the oxygenator during Phase 1 for all six dogs, and the oxygen content of arterial blood during Phase 2 for four of them is shown in Fig. 2. Dogs 387 and 390 died before Phase 2.

During Phase 1 the oxygen content was higher in the blood leaving the oxygenator than that in the blood entering the oxygenator, indicating the amount of oxygen added by the oxygenator. During Phase 2 there was a progressive fall of the oxygen content in the arterial blood.

Discussion

A small extracorporeal membrane oxygenator enabled a dog to survive while breathing a lethal gas mixture containing only 10% oxygen. Such a device might be adapted for human use during temporary pulmonary insufficiency. The oxygenator is small and light enough to be carried by ambulatory patients using a shunt similar to that used for hemodialysis. A small container with compressed oxygen would also have to be carried. No attempts have been made to implant the device as suggested by other investigators.[3, 4]

The free hemoglobin concentration increased during extracorporeal circulation; this hemolysis is partly caused by the pump which might not be necessary when the oxygenator is used for patients. A pumpless system has recently been described by Folkman, Winsey and Moghul,[5] though for a different purpose.

In the assessment of a membrane oxygenator the most important measurement is the oxygen transfer rate, that is, the amount of oxygen carried across the membrane per unit time. If the difference in oxygen content between the blood entering and leaving the oxygenator is 4 vol. % at a flow rate of 50 ml./min., only 2 ml. of oxygen are added per minute. Although we did not measure the oxygen consumption of the dogs during the experiment, it is said to be 6 to 8 ml./kg./min.[6] Since our dogs weighed 10 to 15 kg., the amount of oxygen provided by the oxygenator is only a small fraction of the total oxygen consumption.

Fluctuations in the oxygen concentration were observed at different times in different animals. For this reason the oxygen concentration in the individual experiments are reported instead of the average of the whole group. The oxygen concentration in the first five dogs (no temperature control) showed similar variations. They are of questionable value because of the hypothermia and are not reported.

It is difficult to design an experiment to demonstrate whether or not the oxygenator has maintained the life of the experimental animal during the hypoxic period. The minimal amount of oxygen necessary to maintain life depends on many factors and some of these may vary during a given period of hypoxia. Since the blood flow is from artery to vein, the mechanical pump does not lessen the work of the heart, as in veno-arterial pumping, in fact it may increase it. The pump is used solely to keep the flow constant during the experiment.

In controlled experiments the mortality rate was the most significant index of the usefulness of the tubular membrane oxy-

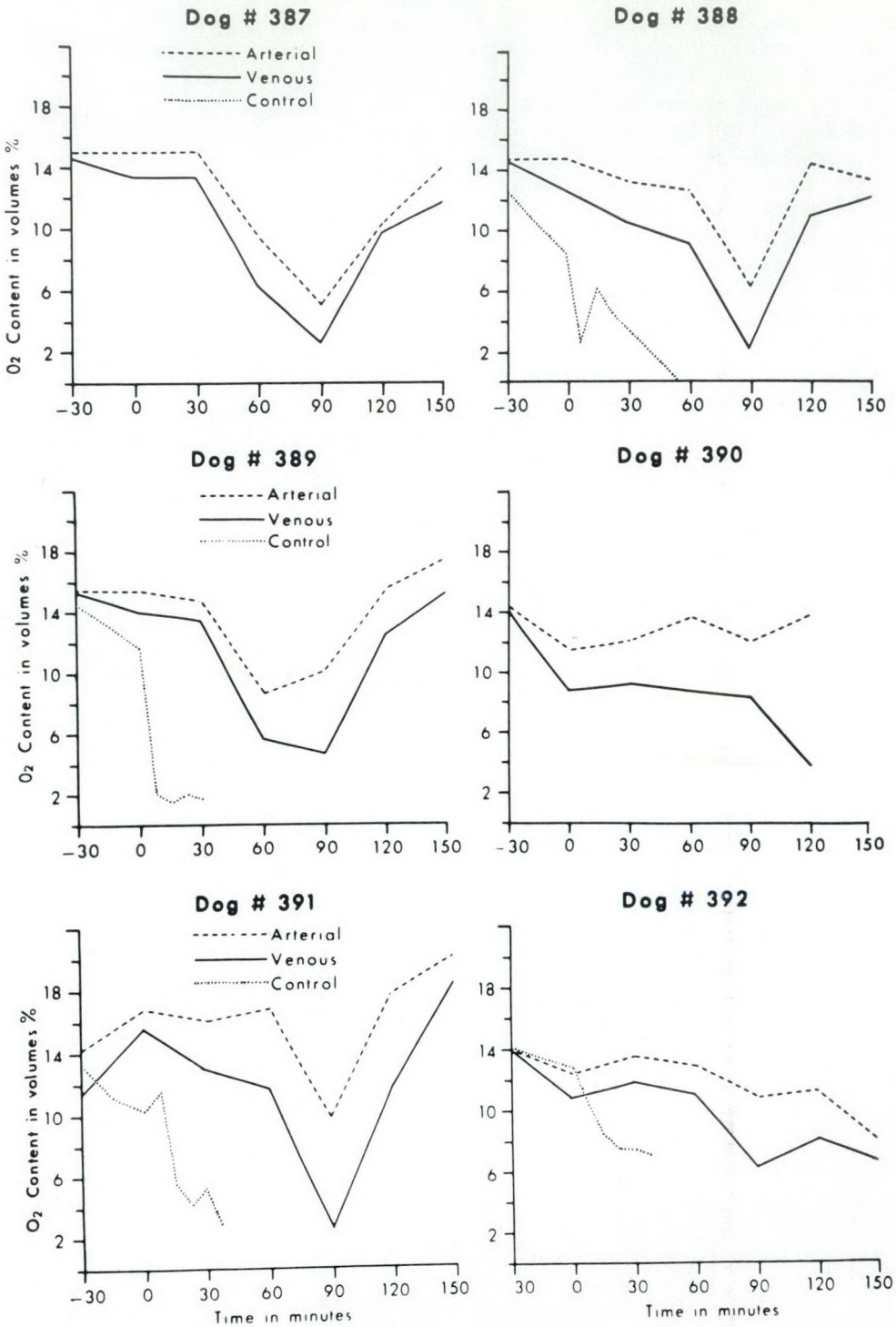

Fig. 2.—Oxygen content in the blood entering and leaving the oxygenator in Phase 1, and in arterial blood in Phase 2. The oxygen content of the respired gases is gradually reduced during the first 30 minutes: the hypoxic gas mixture is maintained starting at time 0 for 2½ hours.

genator as an auxiliary lung. Although we cannot state with certainty that the addition of a small amount of oxygen to the circulation of animals breathing a hypoxic mixture of gases has been life-saving, the addition of an auxiliary lung may be useful. If in patients still more oxygen is necessary, a larger oxygenator or a more efficient one can be developed.

Kolobow, Zapol and Pierce[7] recently used a veno-venous bypass in newborn lambs for a period of one week with good results. Apparently this type of bypass was well tolerated for long periods and may be of value in the treatment of temporary pulmonary deficiency. One problem yet to be solved is intravascular clotting. The use of non-thrombogenic materials, such as heparin-treated membranes, in the construction of the oxygenator may make anticoagulation unnecessary.[8]

In our series two dogs died. Dog 390 (Fig. 2) died during Phase 1 because of an excessive drop in oxygen content, exceeding the capability of the oxygenator. The complication observed in Dog 387 (Fig. 2) is unexplained. He had severe generalized convulsions on the fourth day after the experiment and so was killed with an overdose of pentobarbital. At autopsy no cause for the convulsions was found. The postoperative course of this animal was different from that observed in dogs with hypoxic brain damage.[9]

When a membrane oxygenator is used for total cardiopulmonary bypass, carbon dioxide extraction may be unsatisfactory. But in pulmonary insufficiency the danger is hypoxia and not hypercapnia, so carbon dioxide extraction is not crucial.

As in other membrane oxygenators, because of preferential streaming some of the blood flowing through the oxygenator may be excluded from contact with the membrane. Since the oxygenator is pliable and compressible, the stationary layers of blood[10] can be broken up and returned to the circulation. The best way to break up these layers is to squeeze the oxygenator rhythmically by hand, because it does not lead to an increase in free hemoglobin. We hope to design a mechanical device which will prevent preferential streaming and make hand manipulation unnecessary. When this has been achieved, we can increase the length of time the oxygenator can remain in the circulation.*

Summary

A small membrane oxygenator, originally designed for total bypass in infants, was used as an auxiliary lung in dogs breathing a lethal hypoxic gas mixture. Each animal was first subjected to a period of hypoxia during which the membrane oxygenator added oxygen to the circulating blood via a partial bypass system (Phase 1). Two to three weeks later, the dogs breathed the same gas mixture without oxygen added by the oxygenator (Phase 2). Eleven of 13 dogs survived Phase 1, but none survived Phase 2. The amount of oxygen added to the circulation was small, but seemed to be significant under hypoxic conditions.

References

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*Since the preparation of this paper, similar results have been reported by Frater, Wexler and Amirana[11] and by Awad *et al.*,[12] the latter using a disc oxygenator.

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Résumé

Un oxygénateur à membrane, de dimensions réduites, a servi de poumon auxiliaire à des chiens respirant un mélange gazeux contenant seulement 10% d'oxygène. Cet appareil, à l'origine, avait été conçu pour maintenir une circulation extracorporelle chez des enfants en bas âge. Chaque expérience fut divisée en deux étapes. Dans un premier temps, chaque animal était soumis à une période d'hypoxie au cours de laquelle le poumon auxiliaire fournissait de l'oxygène à la circulation sanguine par l'intermédiaire d'un système à dérivation partielle (1ère étape). Deux à trois semaines plus tard, l'animal respirait le même mélange gazeux mais cette fois, sans que de l'oxygène soit fourni au système (2ième étape). Onze des treize chiens étaient encore vivants après la première étape mais, aucun n'a survécu à la deuxième étape. La faible quantité d'oxygène ajoutée à la circulation par l'oxygénateur était suffisante sous des conditions d'hypoxie.

ORTHOTOPIC HOMOTRANSPLANTATION OF SMALL INTESTINE AND RIGHT COLON

In the October 1969 issue of the *Journal de Chirurgie*, nine papers are devoted to the discussion of a 33-year-old North African man suffering from Gardner's syndrome. This hereditary syndrome, first described in 1953, consists of tumours of endodermic origin, usually in the form of a diffused polyposis of the intestinal tract associated with tumours of mesodermal and sometimes ectodermal origin. The patient was admitted for pulmonary tuberculosis, but later intestinal polyposis and a tumour in the mesentery were discovered.

At exploratory laparotomy, the disease involved almost all the small bowel except for 10 cm. of jejunum and 20 cm. of ileum. Concurrent rectocolic polyposis necessitated a complete colectomy. While preparations were being made for a bowel transplant, the condition of the patient deteriorated and he developed signs and symptoms of partial occlusion of the bowel. A donor in coma following an accident supplied the transplant and the transplantation was done on January 22, 1969.

The whole area supplied by the superior mesenteric artery was transplanted. The same surgical technique (described in a separate paper) was used for donor and recipient. The transplant was perfused with a solution containing dextran and cooled to 14° C. The blood supply was interrupted for 50 minutes. The donor's distal superior mesenteric artery and vein were anastomosed to the proximal superior artery and vein of the recipient. The small bowel was anastomosed at the level of the proximal jejunum. A double-barrelled colostomy was formed with the proximal loop of transverse colon of the transplant and the distal loop of transverse colon of the recipient colon.

During the first 24 hours after the operation, the patient complained of severe abdominal cramps and the colostomy produced a litre of clear fluid. Later the pain disappeared. Diuresis was satisfactory. Immunosuppression was started with azathioprine, antilymphocytic serum and steroids. Between the eighth and eleventh days the patient was able to get up and the gastric suction was removed. The colostomy produced fecal material. On the twelfth and thirteenth days, his condition deteriorated and an abdominal mass could be palpated. At reoperation on the fourteenth day, this patient had massive lymphatic infiltration at the root of the mesentery which subsequently was found to be sterile. From the fifteenth to the nineteenth days, the immunosuppressive therapy was intensified. On the twentieth day, the leukocyte count fell to 600/c.mm. On the twenty-third day, the colostomy was necrotic and the patient died 26 days after the operation.

Additional papers in the same issue discuss the gastroenterologic problems encountered in this patient, the anesthesia used and the immunotherapy and describe the postmortem findings.—Olivier, C. *et al.*: Homotransplantation orthotopique de l'intestin grêle et des côlons droit et transverse chez l'homme, *J. Chir.*, **98:** 323, 1969.

A NEW DIAPHRAGM PUMP*

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THIS paper describes a pneumatically operated, 14-ml. stroke volume, diaphragm pump capable of delivering approximately 400 ml. of fluid per minute. This same basic design can also be used to construct units of various sizes.

DESCRIPTION OF THE PUMP

The pump is made from Silastic† or Plexiglass coated with Silastic.§ The inlet and outlet are made of highly polished medical-grade stainless steel (Figs. 1 and 2). The pump has an external diameter of 7.6 cm. and a thickness of 3.7 cm. The pumping chamber, a hollow hemisphere, has a diameter of 3.9 cm. and a radius (depth) of 1.6 cm. An inset "O" ring, with an internal diameter of 4.7 cm., is used to seal the back of the pumping chamber. Four set screws press the back cover and diaphragm against the "O" ring, thereby sealing both the air chamber and the blood pumping chamber (Fig. 3).

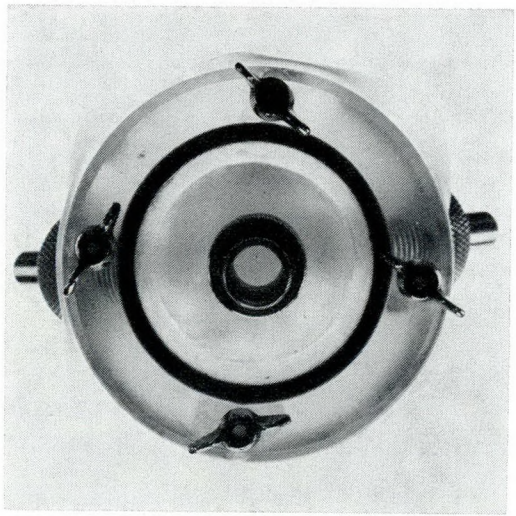

Fig. 1.—Back view of the pump. The wing nuts press both the cover and the diaphragm against the "O" ring, sealing the air and the blood chambers simultaneously.

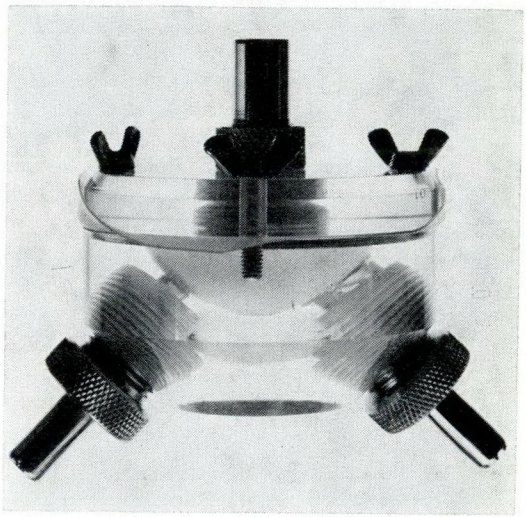

Fig. 2.—Side view of the pump. Note the hemispherical blood pumping chamber.

The blood inlet and outlet tubes, located on opposite sides of the pump, are made from highly polished medical-grade stainless steel tubing with an outer diameter (OD) at the wide end of 1.6 cm. and a 0.9-

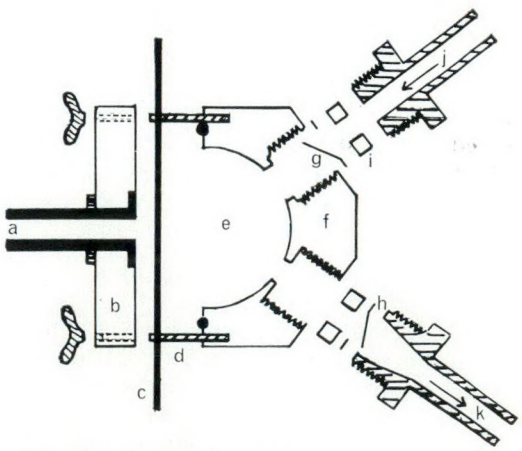

Fig. 3.—Cross-section of the pump. Left to right: (a) air inlet tube, (b) back cover, (c) diaphragm, (d) set screws, (e) pumping chamber, (f) wall of the pumping chamber, (g) flutter valves, (h) anchor, (i) Teflon seals, (j) inlet and (k) outlet tubes.

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†Dow Corning Corp., Midland, Mich.

§Medical adhesive silicone Type A, Dow Corning Corp.

cm. OD at the other end. The outside wall is threaded at its wide end and can be screwed into the wall of the pumping chamber until the flutter valves and Teflon seals are compressed firmly (Fig. 3).

The flutter valves control the direction of flow in the inlet and outlet tubes. These valves, made from Silastic sheeting 0.02 inches thick, have an OD of 1.7 cm. and an inner diameter (ID) of 1 cm. and are supported by a 0.4-cm. anchor. The Teflon seals are 0.4 cm. thick, and have an OD of 1.7 cm. and an ID of 0.6 cm.

To-and-fro movement of the diaphragm does the pumping. At systole, air enters behind the diaphragm, the inlet valve closes while the outlet valve opens, and the diaphragm displaces the blood from the hemispherical pumping chamber. In diastole, air pressure drops behind the diaphragm allowing it to return to its original position by its own elasticity. During this time the inlet valve is open and the outlet valve is closed.

Materials and Methods

Pressures were measured at the inlet and outlet of the pump. The following method was used: T tubes were inserted into the inlet and outlet lines of the pump and N.I.H. cardiac catheters advanced to the level of the non-return valves. The N.I.H. catheter was filled with saline and attached to a Statham transducer.* The pressure curves were recorded on a physiograph.† Because this pump was to be used to introduce blood into the top of a vertical membrane oxygenator,[1] the pressures reported are those that correspond to the height of the lung—40 mm. Hg. Higher pressures were also used to test the action of the valves and to check for leakage.

Results

The level in the reservoir supplying fluid into the inlet of the pump was maintained 10 mm. above the pump in order to create a slight positive pressure in this line. At pump diastole, the negative pressure peaked at −37 mm. Hg, while rising to +10 mm. Hg at systole (Fig. 4). On the outlet side, a peak positive pressure of 80 mm. Hg was seen during early systole, decreasing gradually to 60 mm. Hg during late systole and 40 mm. Hg during diastole.

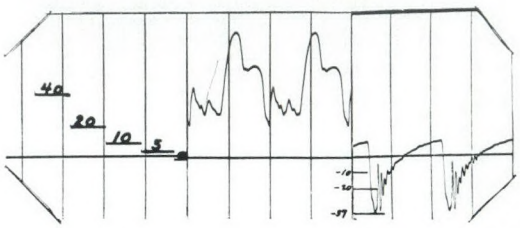

Fig. 4.—Pressures on the left were taken inside the outlet and, on the right, inside the inlet of the pump. Pressures are reported in mm. Hg.

Discussion

During the past year this diaphragm pump has been used daily in the hemodynamics laboratory. It was used to pump blood into the vertical membrane oxygenator.[1] To determine the resistance of the diaphragm and of the flutter valves, we worked them continuously for approximately 200 hours. There were no obvious signs of damage or wear at the end of this period.

The peak negative pressure recorded remained stable through many hours of continuous usage, suggesting that Silastic has an excellent structural memory and returns to its original position after long hours of use.

The rough Silastic coating inside the pumping chamber seems to cushion the extreme displacement of the diaphragm and protects the cellular elements of the blood trapped at the end of systole. The roughness of the coating does not seem to harm the blood cells as evidenced by the small number of cells destroyed by the pump.

Summary

We have described a simple diaphragm pump which is inexpensive to build and simple to use. This pump is rugged and can circulate blood for prolonged periods of time. With certain modifications in this design, pumps of various sizes and flow rates can be built. In assisted circulation,

*Statham Instruments Inc. (P 23AA), Hato Rey, Puerto Rico.

†Electronics for Medicine (DR8), White Plains, New York, N.Y.

this pump could withdraw venous blood and introduce it into an oxygenator. It could also be used for totally implantable circulation assistance.

We would like to thank Mr. F. Lemieux, R.E.T. for his help in designing the pumps and Mr. M. Giguère, R.B.P. for the graphics.

Reference

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Résumé

Les auteurs présentent une nouvelle pompe à diaphragme dont la construction est peu coûteuse et le maniement simple. De construction robuste, cette pompe permet de faire circuler du sang pendant de longues périodes.

Certaines modifications mineures de l'appareil permettent de construire des pompes de diverses dimensions et possédant des débits différents. Dans la circulation assistée, cette pompe a permis de retirer du sang veineux et de l'envoyer vers un oxygénateur. Enfin, cet appareil peut être utilisé dans les cas de circulation assistée entièrement implantable.

BLOOD SUPPLY OF COLON IN ESOPHAGEAL REPLACEMENT

This postmortem study investigates the vascular supply and the anastomotic pattern of the colon, as it would be used for an esophageal replacement. The arterial system was injected through the inferior mesenteric artery or the superior rectal or sigmoid branch. Following injection, the vessels were dissected. In addition, the veins to the left colon were studied. The success or failure of the use of the left colon depends on a satisfactory marginal artery of Drummond. In the most frequently used technique, the only blood supply to this marginal artery is from the inferior mesenteric artery. The incidence of absence of the marginal artery is 4% to 7%. The vessel may be very small in one-third of patients. When this is observed, care must be taken in choosing where to divide the left colic artery. The marginal artery is supplied by the inferior mesenteric artery, and the presence of atherosclerotic changes in the aorta and inferior mesenteric orifice is significant—4 of 27 patients in this series had occlusion of this vessel at its origin.

The simple palpation of this vessel is unreliable because most of the plaques were evident only on opening the aorta. The condition of the mesenteric vessels gave no definite clue as to the patency of its point of origin. The anatomic variation of the venous circulation was stressed. In 3 of 23 patients, the marginal venous anastomosis was absent or inadequate. There were three patterns of drainage of the inferior mesenteric vein. In 17 of 23 patients, it drained into the splenic vein. The next most frequent type was the vein joining the splenic vein at its junction with the superior mesenteric vein; the least common was the inferior mesenteric vein directly draining into the side of the superior mesenteric vein. Marginal vein deficiencies were never seen if the usual pattern of drainage into the splenic vein was present; it was sometimes seen when the inferior mesenteric vein entered the junction of the splenic vein and the superior mesenteric vein, and it was always absent when the mesenteric vein joined the superior mesenteric vein. The venous variants were not related to the arterial configuration which was observed.

The author concludes that if adequate marginal venous and arterial anastomoses are present, a segment of splenic flexure on an inferior mesenteric pedicle is a satisfactory segment for esophageal replacement in young patients. However, in older patients, the chance of occlusion of the inferior mesenteric artery is high. A right colon segment will have a better arterial supply, although it has a greater incidence of deficiencies in its marginal venous anastomoses. Anatomically, a segment of transverse colon and splenic flexure on a middle colic pedicle is the best choice in patients over 50. The 10% to 20% chance of a deficient venous anastomoses in the left colon makes it mandatory to evaluate the venous drainage before division. The anatomy of the inferior mesenteric vein is important in this evaluation.—Rooney, B. P.: Blood supply of colon in esophageal replacement, *Irish J. Med. Sci.*, **2:** 301, 1969.

DEMONSTRATION CHEZ LE RAT D'UN "FACTEUR" GASTRIQUE INHIBITEUR DE LA SECRETION GASTRIQUE*

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En 1939, Brunschwig *et al.*,[1] démontraient que le suc gastrique humain contenait une substance inhibitrice de la sécrétion gastrique du chien porteur d'une poche de Heidenhain. Onze ans plus tard, Blackburn *et al.*,[2] prouvaient que ce facteur d'inhibition était plus abondant chez les malades achlorhydriques que chez les sujets normosécréteurs. La démonstration d'une substance inhibitrice similaire fut faite chez le chien par Hood, Code and Grindlay.[3] De semblables inhibiteurs furent aussi retrouvés dans les sécrétions gastriques porcines,[4] la salive humaine,[5] la salive canine[6] et la lymphe du canal thoracique du chien à jeun.[7]

Le but de ce travail était de démontrer l'existence d'une telle substance inhibitrice dans la sécrétion gastrique du rat. Cette expérience nous semblait d'autant plus importante que dans la plupart des travaux portant sur l'inhibition gastrique, on utilise la sécrétion gastrique du rat au cours de dosages biologiques. La substance inhibitrice a été recherchée dans le suc gastrique de rats normaux ainsi que dans celui des rats traités par la réserpine. Nous avons contrôlé l'influence du poids corporel ainsi que l'influence de la variation de température corporelle sur le volume de secrétion et le débit d'acide gastrique total des rats qui servirent au dosage biologique.

Methodes

Formation des groupes expérimentaux

Sur 100 rats mâles de souche Evans, âgés de 6 à 8 semaines et pesant entre 75 et 125 g, la technique de Shay fut pratiquée.[8, 9] Par une table de nombres aléatoires, les animaux furent répartis au hasard en cinq groupes de 20; lors des mesures, ils étaient à jeun depuis 48 heures mais avaient pu s'abreuver à volonté. Les cages avaient un plancher perforé pour prévenir la stercophagie fréquente chez ces animaux à jeun.

Technique de Shay

Le rat anesthésié à l'éther est pesé, sa température rectale prise et une laparotomie pratiquée. L'estomac est exposé, le pylore ligaturé par un brin de soie, puis la paroi est refermée par un surjet en un plan total. Au moment de la suture, on injecte dans la cavité péritonéale la substance à étudier diluée dans un tampon phosphate de pH 7.5. La technique bien exécutée se complète en moins de cinq minutes. Les rats gardés dans des cages individuelles pendant quatre heures, sont privés d'eau et d'aliment. Comme ils secrètent continuellement pendant la phase interdigestive, le volume et le débit d'acide de la sécrétion gastrique sont des variables utiles dans l'étude de substances inhibitrices ou stimulantes. Après quatre heures, la température rectale est reprise et les rats sont sacrifiés par une surdose d'éther. Une nouvelle laparatomie est faite et une pince est appliquée à la jonction œsophagogastrique pour prévenir le reflux et la perte de suc gastrique. L'œsophage et le duodénum sont sectionnés et le contenu de l'estomac vidé dans une éprouvette graduée qui est ensuite soumise à une centrifugation (2000 tpm) pendant 15 minutes. Le surnageant est décanté, son volume mesuré puis le débit d'acide total pour quatre heures est déterminé par une solution d'hydroxide de sodium 0.5N à pH 7.5. La titration est faite avec un appareil automatique Radiometer; les résultats sont exprimés en milliéquivalents (mEq pour quatre heures).

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TABLEAU I.—HÉTÉROGÉNÉITÉ DES GROUPES

Groupe	*Réduction moyenne de la température corporelle (°F)*	*Poids corporel moyen (g.)*
I témoin (sans tampon)	1.1	86.3
II témoin	0.5	101.6
III réserpine	1.4	95.0
IV extrait I	1.1	95.6
V extrait II	1.3	99.1
Coefficient de Fisher (F) Comparaison simultanée des cinq groupes	4.97	18.05
P	<0.05	< 0.001

Traitements à l'étude

Les cinq groupes de 20 rats furent soumis aux cinq traitements suivants:

Groupe I.—ligature du pylore sans plus (groupe désigné *témoin sans tampon* dans les tableaux et figures).

Groupe II.—ligature du pylore et injection intra-péritonéale de 1 ml de tampon-phosphate par 100g de poids corporel *(témoin).*

Groupe III.—ligature du pylore, injection intrapéritonéale de tampon et injection sous-cutanée de réserpine à la dose de 0.02mg/100g de poids corporel *(réserpine).*

Préparation des extraits de suc gastrique

Les secrétions gastriques des rats des Groupes II et III ont servi à la préparation des extraits de suc gastrique. Après collection, la sécrétion gastrique a été dialysée dans un sac de matériel synthétique semi-perméable, placé pendant 48 heures dans un courant d'eau froide. Le liquide fut ensuite soumis à la lyophylisation à froid et à vide. La poudre ainsi obtenue fut conservée au congélateur. Elle fut utilisée en suspension dans un tampon phosphate 1.5 molaire à pH 7.5 à une dilution de 2.5mg/ml.

TABLEAU II.—COMPARAISON SIMULTANÉE DES CINQ TRAITEMENTS PAR ANALYSE DE COVARIANCE

Groupe	*X moyen*	*Y moyen*	*Y moyen ajusté*	*F'*	*p*
I Témoin (sans tampon)	86.3	3.69	4.22		
II Témoin	101.6	4.69	4.34		
III Réserpine	95.0	5.38	5.41	44.03	<0.001
IV Extrait I	95.6	2.52	2.52		
V Extrait II	99.1	3.41	3.20		

X = poids corporel (g); Y = volume de sécrétion gastrique (ml).

Groupe IV.—ligature du pylore et injection intrapéritonéale de tampon contenant en suspension 2.5 mg/ml d'extrait de suc gastrique provenant de rats normaux, c'est-à-dire des rats du Groupe II *(extrait I).*

Groupe V.—ligature du pylore et injection intrapéritonéale de tampon contenant en suspension 2.5mg/ml d'extrait de suc gastrique provenant de rats réserpinés, c'est-à-dire de rats du Groupe III *(extrait II).*

Température corporelle

La température rectale prise par télé-thermomètre fut enregistrée pour tous les rats à deux reprises, soit au moment des deux anesthésies à quatre heures d'intervalle.

RÉSULTATS

Variation de la température corporelle (Tableaux I et II)

Entre la première et la deuxième anesthésie, le plus souvent, la température

TABLEAU III.—Corrélations

X	*Y*	*R**	*t*†	*p*
Réduction de la température corporelle (°F)	Volume de la sécrétion gastrique (ml)	0.04	0.41	N.S.
	Débit d'acide gastrique total (mEq)	0.01	0.12	N.S.
Poids corporel (g)	Volume de la sécrétion gastrique (ml)	0.43	4.63	<0.001
	Débit d'acide gastrique total (mEq)	0.36	3.78	<0.001

*Coefficient de corrélation intra-groupe $= R = \sum xy / \sqrt{\sum x^2 \sum y^2}$

†$t = R\sqrt{\frac{n-2}{1-R^2}}$, $dl = 94$

corporelle des animaux diminue; les réductions moyennes varient de 0.5° à 1.4° F. Cette variation n'est pas aléatoire entre les groupes qui diffèrent de façon significative: à l'analyse de variance, le coefficient de Fisher (F) pour la comparaison simultanée des cinq groupes est de 4.97 ($p < 0.05$). Si cette variation dans les réductions de température avait une influence sur la secrétion gastrique, comme elle n'a pas été contrôlée de façon directe, elle introduirait un biais dans nos conclusions (Tableau I). Pour évaluer l'influence de la température sur la sécrétion gastrique, il nous fallait donc rechercher s'il y avait association entre, d'une part la réduction de température corporelle et d'autre part le volume de la secrétion gastrique et le débit d'acide gastrique total. Sur les cinq groupes de 20 rats, nous n'avons retrouvé aucune corrélation entre ces phénomènes. Le coefficient de Pearson (R) intra-groupe est de 0.04 et de 0.01. On peut donc négliger dans le traitement des données la variation de la température qui, dans nos conditions expérimentales, est sans effet sur la sécrétion gastrique.

Variation de poids corporel (Tableaux I et III)

Il en est tout autrement du poids corporel qui diffère de façon significative entre les groupes de rats et qui surtout est en corrélation directe et significative avec le volume de la sécrétion gastrique ainsi que le débit d'acide gastrique total. Plus le rat est lourd, plus élevé est le volume de sa sécrétion gastrique ainsi que son débit d'acide gastrique total. Dans ces deux cas, les coefficients de corrélation respectivement de 0.43 et de 0.36 sont très significatifs ($t = 4.63$ et $t = 3.78$): nous pouvons affirmer l'existence de corrélation avec un risque d'erreur inférieur à 0.001. Il faut donc dans le traitement des résultats constamment tenir compte du poids corporel des animaux; ce que nous avons fait par analyses de covariance.

TABLEAU IV.—Volume de Secretion Gastrique: Analyse de Covariance

Comparaison					
Premier terme	*Moyenne (ml)*	*Deuxième terme*	*Moyenne (ml)*	*Coefficient de Fisher (F')**	*p*
Extrait I	2.52	Témoin	4.34	53.82	<0.001
Extrait II	3.20	Témoin	4.34	22.66	<0.001
Extrait I	2.52	Extrait II	3.20	8.15	<0.01
Réserpine	5.41	Témoin	4.34	18.33	<0.001
Témoin (sans tampon)	4.22	Témoin	4.34	0.14	N.S.

$$*F' = \frac{(\bar{x}'_1 - \bar{x}'_2)^2}{CM'_E \left[\frac{1}{N_1} + \frac{1}{N_2} + \frac{(\bar{X}_1 - \bar{X}_2)^2}{\sum x_E^2}\right]}$$

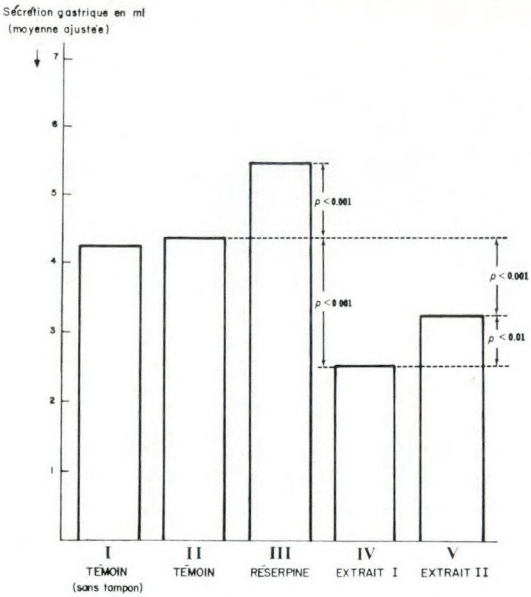

Fig. 1.—Effet des traitements sur le volume de la sécrétion gastrique.

Influence des extraits de suc gastrique sur le volume de sécrétion gastrique (Tableaux II et IV, et Fig. 1)

Il existe une hétérogénéité hautement significative entre les cinq traitements: la comparaison simultanée des groupes produit un coefficient de Fisher (F′) de 44.03 ($p < 0.001$). Les moyennes des volumes de sécrétion gastrique ajustées en fonction de leur régression sur les poids corporels des rats sont de 4.34 ml pour les témoins, de 2.52 pour le groupe extrait I et de 3.20 pour le groupe extrait II. Les extraits de suc gastrique de rats normaux comme de rats réserpinés réduisent de façon hautement significative ($p < 0.001$) le volume de sécrétion gastrique de rat. L'extrait de suc gastrique de rats normaux est plus inhibiteur que celui de rats réserpinés ($F = 8.15$, $p < 0.01$). Par rapport aux témoins, le groupe réserpine montre l'effet stimulant classique de cet alcaloïde ($F = 18.33$, $p < 0.001$). La comparaison des deux groupes témoins n'apporte cependant aucune indication d'un effet du tampon phosphate.

Influence des extraits de suc gastrique sur le débit d'acide total du sac gastrique pour quatre heures (Tableaux V et VI, et Fig. 2)

Les effets des traitements sur le débit d'acide total de la sécrétion gastrique sont en tous points semblables à ceux précédemment décrits sur le volume de suc gastrique. Les cinq groupes sont différents ($p < 0.001$); la stimulation par réserpine est clairement démontrée ($p < 0.001$); l'extrait II est moins efficace que l'extrait I ($p < 0.01$) mais tous deux inhibent le sécrétion gastrique et réduisent le débit d'acide total du suc ($p < 0.001$). Aucune différence statistique n'est retrouvée entre le groupe témoin sans tampon et le groupe témoin.

Discussion

La ligature du pylore associée à l'injection intrapéritonéale d'extrait de suc gastrique n'a pas provoqué d'élévation de température corporelle chez les rats. Au contraire, il fut constaté, ce qui confirme les conclusions de Semb,[10] des réductions de température. Dans les limites de variations de l'expérience, ces réductions sont par contre sans relation statistique avec les variables mesurées. Il reste possible que des réductions plus marquées que 2° F aient une influence sur la sécrétion gastrique.

TABLEAU V.—Comparaison Simultanée des Cinq Traitements par Analyse de Covariance

Groupe	*X moyen*	*Y moyen*	*Y moyen ajusté*	*F′*	*p*
I témoin (sans tampon)	86.3	0.42	0.47		
II témoin	101.6	0.53	0.49		
III réserpine	95.0	0.69	0.69	77.61	<0.001
IV extrait I	95.6	0.22	0.22		
V extrait II	99.1	0.34	0.32		

X = poids corporel (g); Y = débit d'acide total (mEq pour quatre heures).

TABLEAU VI.—Débit d'Acide Total: Analyse de Covariance

Comparaison					
Premier terme	*Moyenne (mEq)*	*Deuxième terme*	*Moyenne (mEq)*	*Coefficient de Fisher (F')**	*p*
Extrait I	0.22	Témoin	0.49	81.11	<0.001
Extrait II	0.32	Témoin	0.49	37.12	<0.001
Extrait I	0.22	Extrait II	0.32	11.88	<0.01
Réserpine	0.69	Témoin	0.49	43.33	<0.001
Témoin (sans tampon)	0.47	Témoin	0.49	0.38	N.S.

$$*F' = \frac{(\overline{Y}_1' - \overline{Y}_2')^2}{CM_E' \left[\frac{1}{N_1} + \frac{1}{N_2} + \frac{(\overline{X}_1 - \overline{X}_2)^2}{\sum x_E^2} \right]}$$

L'effectif relativement faible des échantillons et l'étalement de l'expérience dans le temps ont favorisé l'apparition de différences significatives entre les groupes expérimentaux quant au poids corporel des animaux. En exprimant les mesures de la sécrétion gastrique en ml/100 g ou en mEq/100 g de poids, on éliminerait de façon incorrecte les variations de poids qui influencent les variables mesurées pour les besoins de l'étude. L'analyse de covariance qui tient compte à la fois des variations réelles des poids, des variations des mesures de sécrétion et de la régression de cette dernière variable sur la première, doit être préférée à l'utilisation fautive des quotients ml/100 g ou mEq/100 g.

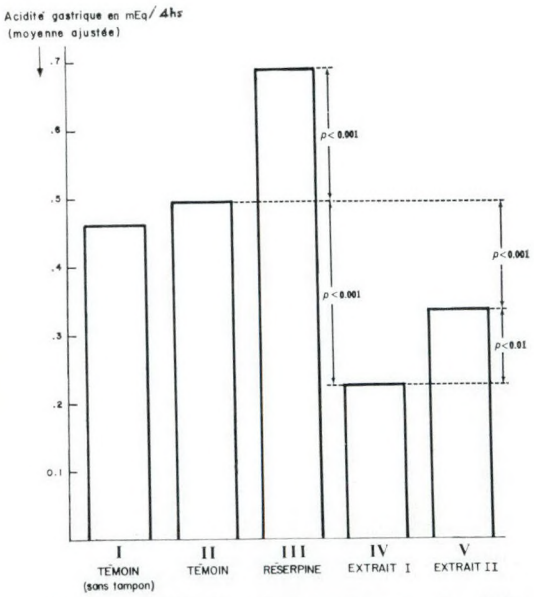

Fig. 2.—Effet des traitements sur le débit d'acide gastrique.

L'extrait de suc gastrique de rats réserpinés est moins efficace que celui de rats normaux. La réserpine stimule peut-être la sécrétion gastrique en réduisant la sécrétion d'un facteur inhibiteur hypothétique ou tout simplement, en stimulant de façon directe la sécrétion gastrique, elle augmente la quantité de substances solides dans cette sécrétion et dilue ainsi la ou les substances inhibitrices de l'extrait.

L'expérience fut assez sensible pour démontrer la stimulation de la sécrétion gastrique par la réserpine et son inhibition par l'extrait de suc gastrique. Dans les mêmes circonstances, il ne fut cependant retrouvé aucun effet du tampon phosphate. Celui-ci n'influence pas la sécrétion; il peut par contre favoriser l'absorption du facteur inhibiteur. Pour conclure à ce sujet, il faudrait étudier l'activité d'extraits de suc gastrique injectés avec et sans tampon. L'influence du suc gastrique est une autre source de variation qui accroît l'erreur expérimentale des études dans lesquelles la technique de Shay *et al.*[8] est utilisée.

A la suite des résultats rapportés, il pourrait sembler convenable de conclure que l'estomac de rat secrète un facteur exocrine qui inhibe la sécrétion gastrique du même animal et qui joue un rôle dans un mécanisme physiologique d'auto-régulation. Une telle conclusion dépasserait largement la portée réelle de l'expérience. Tout ce qui fut démontré, c'est que des extraits de suc gastrique de rat obtenus selon les méthodes que nous avons décrites et injectées dans la cavité péritonéale du rat, inhibent le volume de secrétion gastrique ainsi que son débit d'acide total.

Les extraits de suc gastrique contiennent donc une ou plusieurs substances inhibitrices de nature encore inconnue. Il est possible que ce facteur inhibiteur ne soit qu'un artefact apparu pendant les quatre heures de collection du suc gastrique ou pendant la préparation de l'extrait. Il peut s'agir d'une substance qui existe normalement dans l'estomac et qui n'a d'action sur la sécrétion gastrique que lorsque introduite de façon artificielle dans la cavité péritonéale; ces propriétés n'auraient alors rien de physiologique.

Si ce facteur n'est pas un artefact, que peut-il être? Une sécrétion exocrine de la muqueuse gastrique, une hormone locale qui a diffusé dans le suc gastrique, une hormone normalement sécrétée dans le sang mais qui à cause des techniques expérimentales se retrouverait dans le suc gastrique ou même un produit dû à l'inflammation si minime, soit-elle provoquée par la technique de Shay? L'expérience ne fournit aucune indication qui permet d'émettre avec sécurité une opinion sur la nature de ce facteur inhibiteur. Artefact ou substance naturelle, il est actif lorsqu'injecté dans la cavité péritonéale. Il agit probablement après absorption et transport sanguin. Il reste à prouver qu'il peut être efficace de façon directe après injection dans la lumière de l'estomac. Le site d'action semble être la cellule pariétale puisque le volume et le débit d'acide total sont réduits. On n'a cependant pas pu exclure une action qui ne serait que toxique ou indirecte, par exemple sur la circulation locale de l'estomac. Il reste à faire de nombreux travaux avant de se permettre de spéculer sur le rôle physiologique ou physiopathologique éventuel de ce facteur ou sur son identité chimique.

Résumé

Cent rats (Evans), après ligature du pylore (Shay) furent répartis au hasard en cinq groupes d'effectifs égaux: (I) témoins; (II) témoins ayant reçu intra-péritonéal une solution de tampon phosphate à pH 7.5 (1 ml/100 g); (III) rats traités par le même tampon et une injection sous-cutanée de réserpine (0.02 mg/100 g); (IV) rats traités par le tampon contenant en suspension (2.5 mg/ml) un extrait de suc gastrique de rats normaux, obtenu par centrifugation, dyalise et lyophylisation; (V) rats traités de la même façon par un extrait de suc gastrique provenant de rats réserpinés. Pendant quatre heures le volume de sécrétion (cc) et le débit d'acide total (mEq) furent mesurés. Dans les limites des variations constatées, la réduction de température corporelle n'a aucun lien statistique avec la sécrétion gastrique; il en est tout autrement du poids corporel. En tenant compte de celui-ci par analyse de covariance, il est démontré ($p < 0.001$) que les extraits de suc gastrique inhibent la sécrétion gastrique. L'extrait provenant de rats réserpinés est moins efficace que celui des rats non traités. L'expérience est assez sensible pour détecter ces effets inhibiteurs ainsi que l'effet stimulant classique de la réserpine; on ne retrouve cependant aucune différence significative entre les deux groupes-témoins pour lesquels le tampon reste sans effet.

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Summary

After pyloric ligation (Shay), 100 rats of the Evans type were divided at random into five equal groups: (1) control rats; (2) control rats injected intraperitoneally with a phosphate buffer pH 7.5 (1 ml./100 g.); (3) same as (2) and receiving a subcutaneous injection of reserpine (0.02 mg./100 g.); (4) rats injected intraperitoneally with a buffered suspension (2.5 mg./ml.) of an extract prepared from the gastric juice of normal rats after centrifugation, dialysis and lyophilization; and (5) rats injected intraperitoneally with a buffered suspension of an extract prepared from the gastric juices of reserpine-injected rats.

After four hours, we measured the volume (ml.) and total acid output per four hours (mEq./4 hrs.) of the rats' gastric juices. Within the observed variations, reduction in body temperature showed no statistical relationship to the gastric secretion, but the body weight did. When taking this latter factor into consideration using covariance analysis, we showed ($p < 0.001$) that the gastric juice extracts inhibited gastric secretion. The extract from reserpine-injected rats is less active than that from untreated ones. The preparation is sensitive enough to detect these inhibitory effects as well as the classic stimulatory action of reserpine. There is no significant difference between the two control groups, i.e. the buffer has no effect on gastric secretion.

CLOSED TRAUMA OF KIDNEY

Until a few years ago, non-surgical treatment of closed trauma of the kidney was an established procedure. Surgical intervention was only undertaken when hemorrhage was uncontrollable and was limited to the control of hemorrhage by nephrectomy.

While this attitude saved a large number of kidneys, it should be recognized that, whereas the patient appeared to have recovered from his injury, the kidney often did not regain its function, or it deteriorated secondarily. In a recent series of 20 patients with renal injury with an extended follow-up, the authors had to perform five secondary operations, including three nephrectomies.

They report a closed renal injury to a 19-year-old man. In view of the present management of closed injury to the kidney and on the basis of this man's treatment, the authors sought to establish which kidneys should be operated upon and the time after trauma when the procedure should be undertaken.

Ten hours after an automobile accident this patient was explored because the physical signs suggested a rupture of the spleen. Before this operation they knew he had a renal injury because of massive hematuria. The spleen was not injured, but on palpation of the retroperitoneal renal area, a small hematoma in the lower kidney region was discovered. Because of its size, the peritoneum was not opened, and it was believed that the lesion would heal spontaneously. Neither urography nor renal nor splenic aortography was used before the initial exploratory operation. On the sixth postoperative day, intravenous urography revealed that only the superior portion of the kidney was functioning. The patient continued to have hematuria intermittently. Twenty days after the accident, selective left renal angiography showed that a complete rupture of the kidney had occurred, but that the upper portion of the kidney had retained its normal blood supply.

As a result of the angiographic studies and because of the persistent blood loss, they did a second operation six weeks after the injury. The approach to the kidney was through a classic lumbar incision. Extensive fibrosis made the exploration and the attempted removal of the functioning upper pole of the kidney extremely difficult. However, it was believed that the nephrectomy of the upper pole had been complete. After operation, a urinary fistula developed that drained from 500 to 1000 c.c. of bloody urine a day. An attempt to eliminate the urinary fistula by a ureteral retention catheter was unsuccessful.

The final operation, nearly three months after the injury, was performed through a thoracophrenolaparotomy. Because the spleen was extensively involved in fibrosis by this time, it was removed along with the remaining portion of the kidney. The postoperative course was uneventful.

Because of lessons learned with this patient, the authors stress the importance of complete roentgenograms as soon as possible after the suspected renal injury. Intravenous urography will give valuable information as to the condition of the uninjured kidney as well as to the status of the injured one.—Viville, C., Gillet, M. and Morand, G.: Ce qu'il ne faut pas faire dans le traitement des traumatismen fermés du rein, *Acta Urol. Belg.*, **37**: 267, 1969.

RESPONSE OF CANINE GASTRIC MUCOSA TO HISTAMINE FOLLOWING EXPERIMENTAL IMPAIRMENT OF THE GASTRIC MUCUS BARRIER*

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MUCOSUBSTANCES secreted by the stomach are derived from the columnar cells of the surface epithelium, from the mucous neck cells of the gastric glands and from the mucous cells of the cardiac and pyloric glands.[1] The total of these secretions is referred to as "gastric mucin", and the thin layer of slimy, viscous, translucent or opalescent, slippery mucus covering the epithelial mucosa of the stomach as the "mucus barrier". Because gastric mucin is adhesive, cohesive, viscous and can form gels, it forms a continuous layer separating the underlying epithelium from the proteolytic stomach content.[2-4] Many authors consider that the adsorptive capacity, antipeptic activity and acid-binding capacity of gastric mucus also protect the stomach against digestion.[5, 6] Long ago it was suggested that the visible mucous layer in the stomach protects gastric mucosa against peptic digestion.[7-9] In our time, Hollander[10] described a double protective barrier comprised of secreted mucin and superficial cells. Qualitative and quantitative deficiencies of gastric mucus, found clinically or produced experimentally, were frequently associated with peptic lesions of gastric mucosa.[2, 3, 11-16]

In the present experiment, we induced a deficiency of gastric mucus and then exposed the non-protected stomach mucosa to juice of high acidity, assuming that reduction of the mucus barrier would lower the physiologic resistance of gastric mucosa to peptic digestion. In this study, gastric mucus was washed out from the canine Heidenhain pouch with a hypertonic solution of sodium chloride, using the technique of Webster.[17] This procedure removes the visible mucus and may exhaust the mucin-producing cells.

METHODS

Heidenhain fundic pouches were constructed in 14 dogs (body weight 17 to 22 kg.) and fitted with stainless steel cannulas. Two weeks later, under light sodium pentobarbital anesthesia, the pouches were washed out with normal (0.15 M) or hypertonic (2 M) saline and histamine-stimulated gastric secretion was collected. According to Webster,[17] washing the gastric mucosa with 2 M NaCl removes superficial mucus and exhausts the mucin-producing cells of the surface epithelium. Webster used this "washing out" to collect gastric mucus from canine gastric pouches; we used it to induce a deficiency of the mucus barrier. We introduced from 180 to 185 ml. of saline solution (37° C.) into the pouch through the cannula and left the fluid in the closed pouch for two hours. The saline was then recovered quantitatively and kept for biochemical studies. Immediately after the pouch was emptied, a six-hour infusion of histamine was begun.

For histamine infusion a polyethylene catheter was introduced through an incision in a femoral artery and the tip passed above the celiac axis in the aorta. Histamine dihydrochloride dissolved in normal saline was infused at a steady rate of 3 ml./min. in a dosage of 2 μg./min./kg. body weight. The pouch was emptied at hours three and six of the infusion period. The dogs were protected against a systemic reaction to the histamine by promethazine (Phenergan) given subcutaneously in a dose of 1 mg./kg. body weight at hours zero, two and four of the six-hour stimulation period.

The dose of histamine used was considered sufficient to produce maximal stimulation of canine parietal cells.[18] Instead of the single-dose method, we used the more effective histamine infusion, which provides a steady stimulus to both parietal and chief cells at high doses.[19, 20] Intra-arterial infusion produces a much

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higher rate of gastric secretion than intravenous infusion of a similar dose.[21]

Washing and pooled six-hour secretion of the pouches were studied biochemically in every dog. Gastric juice was titrated in 1.0- or 0.5-ml. aliquots, using a radiometer Type TTT1 titrator, TTA 3 titration assembly and Type AB01 Auto-Burette unit. The pH was read and the sample was then titrated with 0.1 NaOH to pH 7. Pepsin was determined by a modified Anson's method.[22, 23]

To prepare the "dry mucus", each sample of washing or gastric juice was first homogenized at a slow speed (to avoid foam formation) for four minutes at 4° C. The homogenized sample was then dialyzed in cellophane tube for 24 hours against distilled water at 4° C. The non-dialyzable material was shell frozen and lyophilized (freeze-dried) for 24 hours. The freeze-dried material was weighed and used for biochemical study.[24]

With respect to controls, we considered using dogs with 2 M NaCl gastric wash but no histamine as controls. We believe our results provide evidence pointing to post-histaminic hypersecretion as the factor that causes mucosal injury in the pouches deprived of "mucus barrier". The infusion of saline instead of histamine would probably not provoke sufficient, or any, secretion of low-pH gastric juice.

In this experiment we have histamine-stimulated controls washed with normal saline, and a histamine-stimulated experimental group washed with hypertonic NaCl. These two groups are compared and the parameter studied is the presence or absence of protective mucus barrier.

Supplementary controls were done for histologic study, to exclude gastric mucosal damage before gastric stimulation and to ensure that any changes were due only to the washing out of the protective layer of mucus.

TABLE I.—Composition of Washing Fluid Kept in Heidenhain Pouch for Two Hours and Recovered Quantitatively

Initial washing fluid			*Fluid removed from the pouch*										
Composition	*Volume (ml.)*	*No. of pouches*	*Vol. (ml.)*	*pH*	*HCl (mEq./l.)*	*HCl (mEq.)*	*Pepsin (mg.)*	*Dry mucus (mg.)*	*Total protein (mg.)*	*Sialic acid (mg.)*	*Hexose (mg.)*	*L-fucose (mg.)*	*Hexosamine (mg.)*
0.15 M NaCl	182	6	180	3.6	4.8	0.80	30	45.1	29.2	0.86	3.31	0.34	0.99
2 M NaCl	183	8	241	8.1	0	0	176	1218.1	682.4	11.28	47.53	7.82	22.40
P	NS		<0.01	<0.01	—	—	<0.01	<0.001	<0.001	<0.01	<0.01	<0.01	<0.001

Hexosamine,[25] L-fucose,[26] sialic acid,[27] hexose[28] and total protein[29] were determined in the washings and in six-hour pouch secretions of all dogs. The Wilcoxon rank sum test was used for the statistical analysis of biochemical data.[30]

In all animals, the pouches were excised under sterile surgical conditions at the end of the juice collections. The abdomen was closed by the usual method. The mucosa of every pouch was examined macroscopically and histologically. Tissues were fixed in 10% formol saline, embedded in paraffin and cut at 5 μ. Sections were stained with hematoxylin and eosin. Routine histochemical reactions for mucosubstances were also performed. The periodic-acid-Schiff (PAS) stain was used to identify neutral glycoproteins. Iron containing Mayer's mucicarmin stain was used to identify acid mucopolysaccharides.

Results

Table I shows the composition of washing fluid recovered from the pouches. Hypertonic saline removed significantly greater amounts of fluid, dry mucus and various mucus components from the pouches than did normal saline. Washings from the pouches also contained large quantities of pepsin and total protein.

Table II, which gives the results of analysis of six-hour pouch secretion during continuous intra-arterial histamine stimulation, shows that the gastric juice secreted by pouches washed out with 2 M NaCl was rich in mucus and protein. These pouches secreted more fluid and pepsin, but the concentration of HCl was lower than in those washed with normal saline.

All pouches washed with hypertonic solution before histamine stimulation were

TABLE II.—Secretion From Heidenhain Pouch in Response to Six-Hour Intra-arterial Infusion of Histamine. Pouch Washed With NaCl Solution Before Gastric Juice Collection

		Six-hour pouch secretion										
*Pouch washed with**	*No. of pouches*	*Vol. (ml.)*	*pH*	*HCl (mEq./l.)*	*HCl (mEq./6 hrs.)*	*Pepsin (mg.)*	*Dry mucus (mg.)*	*Total protein (mg.)*	*Sialic acid (mg.)*	*Hexose (mg.)*	*L-fucose (mg.)*	*Hexosamine (mg.)*
0.15 M NaCl	6	168	0.96	139	24.2	55	68.1	47.0	1.59	6.03	0.83	2.90
2 M NaCl	8†	258	1.72	70	18.0	336	1304.7	909.5	17.01	67.02	6.19	25.74
P§		<0.05	<0.01	<0.01	NS	<0.01	<0.001	<0.001	<0.001	<0.001	<0.01	<0.01

*Washing solution left in the closed pouch for two hours, then quantitatively removed before infusion of histamine.
†All Heidenhain pouches washed with 2 M NaCl before histamine stimulation contained acute peptic ulcers.
§P >0.05 =not significant (NS).

found to be damaged at the end of the six-hour experiment. Grossly, the mucosa resembled "acute hemorrhagic gastritis" and all pouches showed edema, congestion, superficial submucosal and subserosal hemorrhagic spots, mucosal erosions and "acute ulcers". Some of these erosions were superficial but some were deep and had diameters of about 6 mm. Histologically, the ulcers had local areas of edema of lamina propria, superficial mucosal necrosis and no red cells in the small vessels. Most ulcers showed leukocytic infiltration. In some ulcers, necrotic changes extended from the mucosa to the serosa of the pouch wall. Nuclear debris was scattered in the craters. These lesions resembled post-histamine gastric lesions in dogs[31] and guinea pigs[32] previously described (Figs. 1 and 2).

On histochemical study the mucosa of pouches contained neutral mucoproteins (PAS-positive mucus) and acid mucopolysaccharides (mucicarmin-positive mucus). These substances were markedly depleted from the mucosa washed with hypertonic saline before six-hour histamine stimulation. Figs. 3 to 6 illustrate these changes in the mucosa of Heidenhain pouches.

To exclude the possibility that 2 M NaCl caused the ulcers we studied a few pouches directly after the washing, but in these, we observed no gross or histologic pathology. The surface of the mucosa was poor in mucus, but there was no edema nor congestion. In contrast with 2 M NaCl-washed pouches, all pouches washed with 0.15 M NaCl and stimulated for six hours with histamine appeared normal macroscopically and histologically at the end of the experiment.

Discussion

Gastric Mucus

Visible mucus forms the external layer of the "protective" gastric mucus barrier. Its internal layer consists of the pre-formed mucosubstances within the juxtaluminal

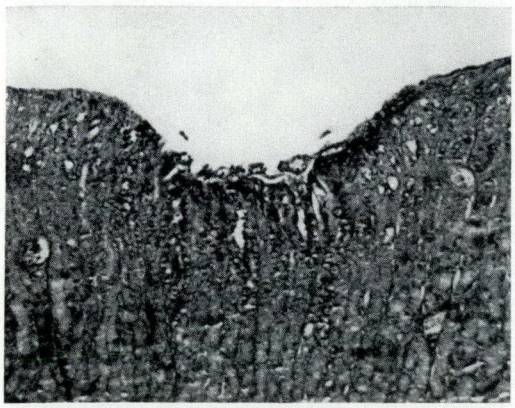

Fig. 1.—A small superficial ulcer of the gastric mucosa in a pouch washed with hypertonic saline before six-hour histamine-stimulated secretion. Necrosis and desquamation of superficial epithelium and mucosal glands (H & E, original magnification × 40).

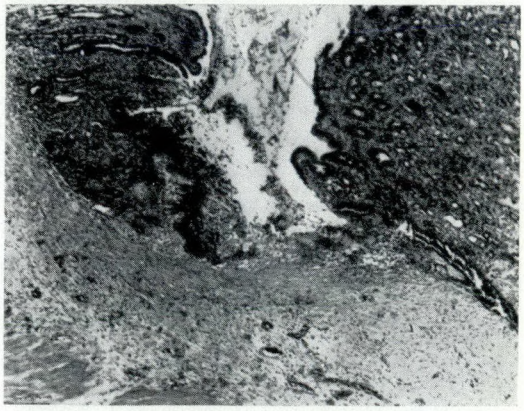

Fig. 2.—Deep peptic ulcer of the gastric mucosa in a pouch washed with hypertonic saline and then stimulated for six hours with histamine. Necrosis reaches the muscularis mucosae; edema and leukocytic infiltration are present (H & E, original magnification × 40).

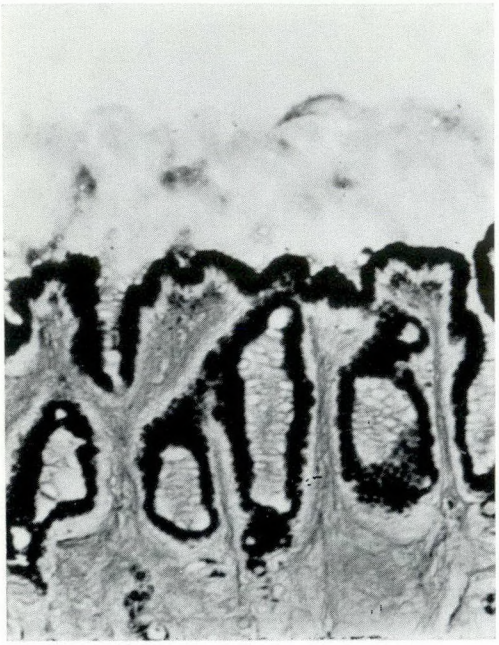

Fig. 3.—Mucosa of a pouch washed with normal saline before six-hour histamine stimulation and collection of secretion. Neutral glycoproteins stained with PAS are present in the surface coat of mucus and in the epithelium (× 100).

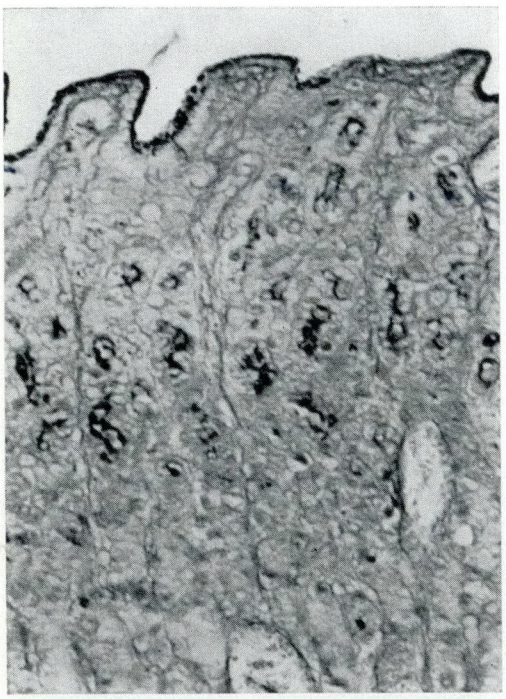

Fig. 4.—Mucosa of a pouch exposed to hypertonic saline before six-hour histamine stimulation and collection of secretion. PAS-stained surface coat of mucus is absent, but a small amount of cellular PAS-positive mucus is present (× 100).

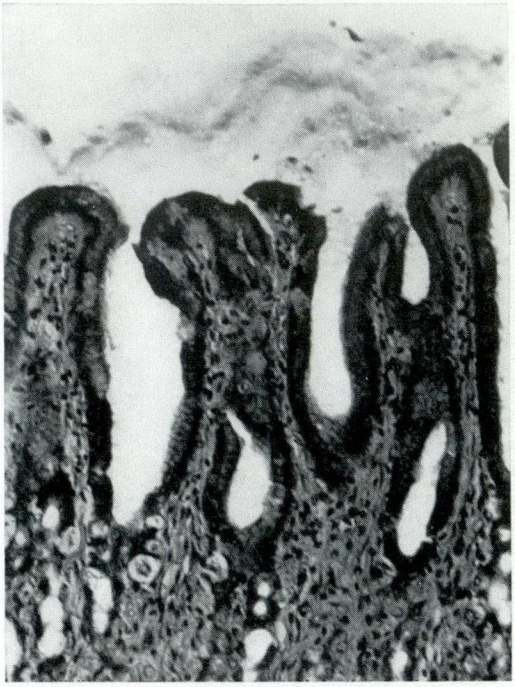

Fig. 5.—Mucosa of a pouch washed with normal saline and then stimulated for six hours with histamine. Acid mucopolysaccharides of mucus are stained with mucicarmin. Mucicarmin-positive mucus is present in the surface coat and in the cells (× 100).

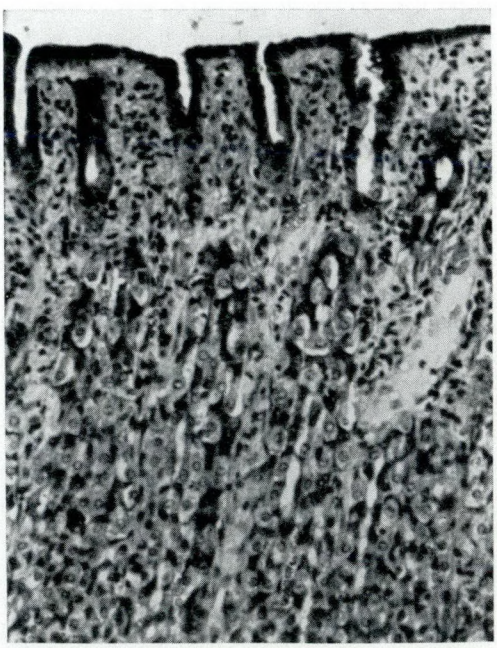

Fig. 6.—Mucosa of a pouch exposed to hypertonic saline and then stimulated for six hours with histamine. There is a decrease of mucicarmin-positive mucus as compared with Fig. 5 (× 100).

portion of the surface epithelial cells.[2, 10] Gastric mucus protects because of such properties as adhesiveness, cohesiveness, viscosity, gel formation and adsorptive capacity.[2] However, some workers believe that the most significant antipeptic activity of mucus is its ability to adsorb pepsin—a process that involves a special antipepsin.[5] Others[2] do not accept this mechanism. Also, the acid-binding capacity of mucus, considered by Hollander[6] to be of major importance, appears to be only of minor significance.[2, 33] It is apparent that the mucus protects the gastric mucosa chiefly by the tenacious layer of mucus which adheres to its surface. Beneath this layer lies the undischarged mucin in the continuous palisade of gastric surface cells, so that the protection afforded by secreted mucus is reinforced by the mucin in the underlying cells. Mucin dissolved in gastric juice does not protect the gastric mucosa and its composition varies markedly, depending upon the stimulus applied to gastric secretion.[2]

According to Webster,[17] the surface epithelium is exhausted by exposing it to 2 M NaCl and large amounts of gel mucin are produced, but the neck cells are not affected. This we have confirmed.

Visible mucus, protecting both the mucosa and the surface epithelium was washed out by hypertonic saline and apparently this decreased the mucus barrier significantly. In pouches washed out with normal saline, the mucus barrier was not damaged and the post-histamine gastric juice did not damage gastric mucosa. In pouches with no mucus barrier, gastric mucosa was damaged by the post-histamine juice, even though the parietal cells of these pouches produced less acid. The mucus barrier was not renewed during the six-hour histamine stimulation period. The mucosa produced large amounts of mucosubstances without being able to reform the protective barrier. Deprived of its protective layer of mucus, gastric epithelium came into direct contact with gastric juice and, as a result, we found severe damage to the mucosa in all pouches so deprived.

Biochemistry of Mucus

Gastric mucins may be classified chemically as mucopolysaccharides, mucoids or mucoproteins, depending on their composition, especially the protein moiety and hexosamine.[2] Eighty per cent of the nondialyzable mucosubstances in gastric mucus is protein.[4] Part of the carbohydrate in gastric mucin belongs to the group of acidic polysaccharides and, of these, sulfated mucopolysaccharides appear to be important components.[3, 34-36] Another part of the mucinous material obtained from gastric juice and gastric mucosa, belongs to the neutral glycoprotein group, which contains glucosamine, chondrosamine, galactose, fucose and fucomucins. The hexosamines together constitute about one-half of the total carbohydrate moiety of gastric mucus.[37] Studies on cellular origin of various gastric mucosubstances have demonstrated that mucous neck cells and parietal cells, and the mucous cells of the surface and crypt epithelium[38] all participate in the secretion of the neutral glycoproteins.

In our experiment, various components of mucus found in both saline washings and posthistamine juice of Heidenhain pouches probably have a mixed origin. Most of the mucus in the 2 M NaCl washings originates from the surface layer and from destroyed surface epithelium.[17] Table I shows the magnitude of the action of hypertonic saline on various components of mucus barrier. If the "washing out" action of 2 M NaCl on mucus is easy to understand,[17] the presence of large amounts of mucosubstances in histamine-stimulated pouches is difficult to explain.

It is not definitely proved that histamine stimulates the secretion of mucus. Previously, in guinea pigs and rats, we found that endogenous histamine, released by a histamine liberator in rats, did increase the content of hexosamine in gastric juice.[39] However, most workers do not believe that histamine stimulates the output of gastric glycoproteins.[40, 41] Others found that, after histamine stimulation, non-sulfated glycoproteins accumulate in the epithelium of the surface and crypts of the stomach[42]—an observation that supports our finding of post-histamine increase of hexosamine content in the gastric wall.[39] However, this work on the effect of histamine on mucus does not explain the finding in the present experiment. Perhaps, in the absence of the

mucus barrier, the remaining mucus cells on the surface and some neck cells were damaged by gastric juice and their mucosubstances were washed out during the stimulated secretion. It is also possible that, under the conditions of this experiment, some of the mucus cells were stimulated by histamine. It is interesting to note that gastric juice obtained from pouches deprived of mucus barrier contained large amounts of protein. Normal gastric secretion contains mucoproteins, mucoproteoses, serum proteins, peptides and various amino acids.[41] Most protein found in the present experiment was derived from gastric mucus: some was probably serum protein. We know that much serum protein leaks into the gastric lumen as exudation from ulcerated mucosa or as transudation from the gastric vessels whose permeability is increased.[43, 44] The conditions necessary for increased exudation of protein were certainly fulfilled in the pouches deprived of mucus barrier and damaged by post-histamine secretion. Also, the vascular permeability of stomach after massive histamine stimulation[45] probably contributed to the transudation of protein into these pouches.

Thus, both histologic and biochemical results of the present experiment indicate that hypertonic NaCl destroyed the mucus barrier and exposed the pouch mucosa to the proteolytic action of post-histaminic gastric secretion. In the present study, we have confirmed the importance of "mucus barrier" as a protective agent, preventing the digestion of normal gastric mucosa. Webster's technique[17] of mucus collection proved to be an ideal tool for the study of the "protective role" of gastric mucus.

Summary

Concentrated sodium chloride introduced for two hours into Heidenhain pouches exhausted the mucin-producing cells of the surface epithelium and washed out the "mucus barrier" considered to protect against acid-peptic digestion of gastric mucosa.

Histochemical and biochemical study showed that large amounts of neutral glycoproteins were removed from the pouches washed out with 2 M NaCl, and that normal saline did not produce such an effect.

After maximal intra-arterial histamine stimulation for six hours, pouches deprived of their mucus barrier secreted gastric juice rich in mucosubstances and in protein, but pouches washed with saline did not.

After six-hour stimulation all pouches previously washed with 2 M NaCl had severe lesions of the gastric mucosa. These lesions we considered were due to the action of gastric juice on mucosa deprived of protective mucus barrier.

After six-hour stimulation all pouches previously washed with normal saline presented gross and histologically normal gastric mucosa. In these pouches the mucus barrier was intact.

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Résumé

La présente expérience avait pour objet d'étudier le comportement de la muqueuse gastrique, privée de son mucus protecteur, en présence de suc fortement acide.

Pour ce faire, les auteurs ont introduit pendant deux heures une solution concentrée de chlorure de sodium dans un petit estomac de Heidenhain, ce qui eut pour effet d'épuiser la sécrétion de mucine de l'épithélium superficiel et d'éliminer la "barrière de mucus" qui est censée protéger la muqueuse gastrique contre son auto-digestion par l'acide chlorhydrique et la pepsine.

L'étude histochimique et biochimique a révélé que la solution de 2M NaCl a éliminé de l'estomac de grosses quantités de glycoprotéines neutres, tandis que la solution normale de NaCl n'avait pas cet effet.

La stimulation maximale de l'estomac par injection intra-artérielle d'histamine, prolongée pendant six heures, a provoqué une sécrétion de suc gastrique riche en mucus et en protéines, mais ceci n'a eu lieu que dans les sacs de Heidenhain privés de leur barrière de mucus et non pas dans les petits estomacs irrigués par le soluté de NaCl normal. Après une période de stimulation de six heures, la muqueuse gastrique des petits estomacs préalablement irrigués avec la solution de 2M NaCl présentait des lésions sévères; nous avons considéré que ces lésions étaient la conséquence de l'action du suc gastrique sur une muqueuse privée de sa barrière protectrice.

Par contre, tous les petits estomacs préalablement irrigués par le soluté salin normal avaient une muqueuse normale, tant au point de vue macroscopique qu'au point de vue histologique. Dans ces estomacs, la barrière protectrice de mucus était intacte.

TRAUMATIC CEREBROSPINAL FLUID OTORRHEA

Cerebrospinal fluid fistulas of the petrotympanic bone require surgical intervention less frequently than those of the frontal or the ethmoid regions because the former are less frequent and have a greater tendency to heal spontaneously than the latter. Drainage which persists for 8 to 10 days or infections which develop regardless of prophylactic measures call for surgical intervention. Since 1959, the authors have encountered seven petrotympanic fistulas which required a total of 13 operations before all were closed. During the same period, they repaired 24 fistulas of the anterior or ethmoid type without the need for a single reoperation.

For fistulas through petrotympanic fractures, the choice of procedure depends upon the location of the fracture. The anterior fracture runs across the tegmen and communicates between the subtemporal region and the middle ear. The posterior fractures traverse the posterior surface of the petrotympanic bone in various ways in the lateral cerebral cistern. These may be divided into: fractures located in front of the internal auditory canal which have not been reported; fractures of the end of the internal auditory canal located entirely within the petrous bone; and fractures located behind the internal auditory canal and extending from the posterior surface of the petrotympanic bone into the posterior fossa.

In the diagnosis and location of these fractures roentgenography is helpful in topographic diagnosis, but may be misleading and may not reveal small fractures. During operation, injection of coloured dyes into the middle ear, the external auditory canal, or the mastoid cells sometimes has aided in locating the internal opening; the authors have used methylene blue for this purpose, but suggest that another dye with antibiotic properties may be more suitable.

Fistulas from fractures of the anterior surface of the petrotympanic bone are readily exposed and repaired through a flap centred over the external auditory canal. Fractures of the posterior surface present a more serious problem. The rarity of fractures of the posterior surface in front of the internal auditory canal suggests that this is not the first place to seek the internal opening of a fistula. Fractures of the end of the internal auditory canal are usually, if not always, beyond the technical limits of the neurosurgeon. All that can be done internally is to pack a little muscle behind the fistula—a futile endeavour which may endanger the acousticofacial nerve.

Otologic techniques consisting of intra-aural tamponade or plombage are the only convenient and effective methods for treating these fistulas, but they also may be ineffective and dangerous. The third type of fracture of the posterior surface of the petrotympanic bone often is accessible by trephining the posterior mastoid cells and also is curable by neurosurgical techniques. Composite temporal and suboccipital approaches which permit exploration of both anterior and posterior surfaces of the petrotympanic bone will reduce the number of reoperations.—Jenny, P. *et al.*: Les otorrhées cérébro-spinales traumatiques; problemes chirurgicaux, *Neurochirurgie*, **15**: 137, 1969.

NEUROFIBROMATOSIS OF BLADDER: CASE REPORT AND REVIEW OF LITERATURE

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NEUROFIBROMATOSIS involving the urinary tract is rare. In 1963 Gonzalez-Angulo and Reyes[1] collected 22 cases, published since Gerhardt's[2] first case in 1878, and added two of their own. The following year, Van Buskirk *et al.*[3] reported one more. This condition was unknown in the French literature until 1963, when Delange[4] wrote his thesis on the subject. In 1966 Bitker *et al.*[5] reviewed the English, French and German medical literature, collected 29 cases, and added two more of their own. A few months later Torres and Bennett[6] added one case to complete the count. (Pessin and Bodian[7] reported six cases studied under the broader heading of pelvic neurofibromatosis.) At least seven cases had no generalized cutaneous lesions suggesting von Recklinghausen's disease;[5, 8, 9] nine were women and 11 were children.[5, 6, 10] The average age of these patients is 30 years.[5]

The patient reported here illustrates that the clinical picture in neurofibromatosis of the urinary tract is non-specific and that the urinary tract may be involved frequently in von Recklinghausen's disease.

CASE REPORT

M.B.B., a 62-year-old white man, was admitted to Notre-Dame Hospital, Montreal, on July 25, 1967, with the chief complaint of urinary frequency (10 x), nocturia (3 x) and moderate urinary incontinence, with varying intensity for the last 10 years. His admission was precipitated by the recent addition of burning on urination and a decrease in the volume of the urinary stream. Incontinence was preceded by extreme urgency and was never of large volume. In 1963 the patient was admitted for hemorrhoidectomy. The urinary incontinence, present then, was treated with anticholinergic drugs and antibiotics with only slight improvement. Other members of his family had no cutaneous lesions suggestive of von Recklinghausen's disease.

He was obese and his whole body was covered with innumerable cutaneous nodules of varying sizes from a few millimetres to 2 cm. in diameter (Fig. 1). Typical *café au lait* patches were present on the trunk and abdomen.

Fig. 1.—Typical cutaneous lesions of von Recklinghausen's disease.

Routine hemogram and blood chemistry determinations were within normal limits. Urinalysis revealed numerous red blood cells per high-power field. Urine culture grew *Pseudomonas aeruginosa* with a colony count of more than 100,000/ml.

Radiographs of the chest, and kidney configurations on the excretory urograms, were normal. Cystography showed a mildly trabeculated bladder with some deformity of the vesical neck presumably caused by prostatic hypertrophy. Cystometric curve was considered normal and he had no significant residual urine. At cystourethroscopy slight trabeculations were seen but the bladder was otherwise

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normal. There was no evidence of tumour or diverticulum. The prostatic urethra showed no significant obstructive pattern from the small lateral lobe hypertrophy. However, the vesical neck was deformed by what appeared to be an irregular median lobe. Transurethral electroresection of the vesical neck was next considered in the hope of smoothing the closure of the vesical neck.

On July 31, 1967, he underwent resection. We were somewhat bewildered by the glistening aspect of the cut sections which suggested fat tissue from perforation. This was most unlikely because all the "chips" from the beginning of the operation had this same appearance and we had not entered a muscular fibrous layer. His postoperative course was uneventful. When the patient left hospital a week later, his urinary symptoms had disappeared except for slight urgency incontinence.

Pathology

The operative specimen consisted of multiple small fragments of fibromuscular tissue some of which were covered by a transitional lining (Fig. 2). There were no prostatic glands but some fragments had mucous glands identical to those normally seen in the posterior urethra. Most fragments were occupied by a neurofibromatous tumour made of interlacing bundles of wavy, edematous, and poorly cellular fibrillar tissue (Fig. 3). Embedded between the fibrils, we found a few oval or spindle-shaped nuclei and numerous mast cells. In some regions, the tumour extended between fat lobules and muscle bundles.

Fig. 2.—Portion of the bladder wall with transitional lining partly ulcerated. The submucosa shows inflammatory cells, dilated capillaries and neurofibromatous proliferations (× 30).

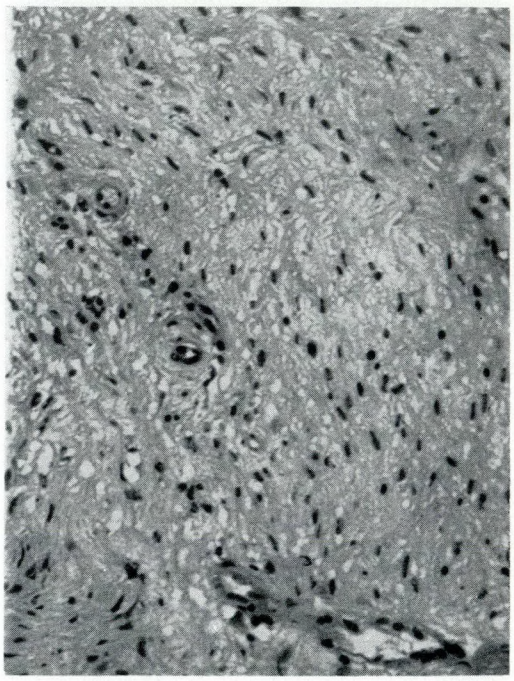

Fig. 3.—High-power view of tumour showing wavy fibrillar tissue and poor cellularity (× 190).

Discussion

Neurofibromatosis (von Recklinghausen's disease), a phakomatosis,[11] is a hereditary and familial disease characterized by multiple cutaneous neurofibromas and cutaneous pigmentation (*café au lait* spots). The tumours probably originate as a connective-tissue reaction of the nerve sheath.[5, 12, 13] Although their location is mostly on the cutaneous nerves, visceral nerve involvement has been reported; the digestive tract being the most commonly affected.[5, 14]

Since Gerhardt's[2] initial report of urinary tract involvement in 1878, few additional cases have been published. The bladder

and more specifically the trigone and vesical neck are the most common sites of occurrence.[5] However, these tumours were also found in the prostate, urethra, spermatic cord, penis,[15] tunica albuginea of testis[16] and ureter.[17] The 32 case reports collected from the literature do not reflect the true incidence of urinary tract involvement because the symptoms are non-specific and may not be very troublesome. Our patient waited 10 years before he consulted a physician about his urinary complaints.

Because of their usual location, these tumours give rise to obstructive symptoms, hindering urethral drainage[18] or bladder evacuation.[1, 4] They may also produce simple dysuria with frequency, and frequency incontinence or incontinence from decreased bladder capacity.[3] The solitary lesion in our patient gave rise to vesical neck irritation. Neurofibromas of the spinal cord or brain producing neurogenic dysfunction were ruled out; there were no objective changes on neurologic examination.

We were puzzled by the presence of abundant fatty tissue in the vesical wall and in a few fragments immediately beneath the mucosa. This fat tissue had a normal appearance and was dispersed in a random fashion between muscle bands and neurofibromatous growths, but there were no circumscribed lipomatous tumours as occasionally seen in von Recklinghausen's disease.[19] It is difficult to explain this phenomenon because we did not have the opportunity to study the whole thickness of the bladder wall. It probably represents secondary fatty infiltration associated with the patient's marked obesity or less probably hamartomatous growths[20] associated with the tumour. This might also represent perivesical fat from over-enthusiastic resection, although there were no clinical signs of perforation.

Malignant changes have been reported[19] in 5% to 16%[21-23] of neurofibromas—a possibility that must be considered in choosing treatment. The obstructive features of some tumours dictate surgical or other resection. Hosoi[22] noted a high incidence of sarcomatous changes in von Recklinghausen's disease after resection. Although radical resection would appear to be rational, the frequent multicentric occurrence of the lesions and their usually benign course should be weighed seriously, especially in poor-risk patients.[5] Simple urinary diversion may well be the proper treatment.

Serious heart disease in our patient precluded additional excision. However, on a two-year follow-up, he has shown no signs of malignant activity on cystoscopic examination. He continues to have slight urgency incontinence and takes anticholinergic medication to control this symptom.

Summary

A 62-year-old white man with neurofibromatosis and generalized cutaneous lesions had localized bladder neck involvement and urinary incontinence.

On transurethral resection, we obtained edematous and highly vascularized tissue, containing cells with spindle-shaped nuclei and elongated cytoplasm typical of neurofibromatosis. The tissue was densely infiltrated by mastocytes. The specimen contained fatty tissue the source of which is discussed.

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Résumé

L'observation clinique que nous présentons consiste dans le 33ème cas de neurofibromatose vésicale notée dans la littérature médicale.

Il s'agit d'un homme de 62 ans avec des lésions cutanées généralisées et typiques de la maladie de Von Recklinghausen. Le malade s'est présenté avec une symptomatologie d'irritation vésicale avec de l'incontinence par mictions impérieuses.

Nous en profitons pour revoir la symptomatologie clinique, l'aspect anatomo-pathologique et l'incidence des observations cliniques de cas semblables.

INTRACRANIAL ANEURYSMS

For many years aneurysms have been treated by wrapping them in a plastic coating. The plastic has characteristics that cause it to adhere rapidly to the aneurysm, forming a casing which will not dilate further. Flexibility and elasticity are other desirable qualities of such a plastic. In addition it must be non-toxic, produce no secondary reaction, be well tolerated by tissue, and be capable of sterilization. The authors have used a material made in Japan known as Aron A-Alpha. The plastic has been used by vascular surgeons with good results.

In a 20-month period, the authors used this material in 10 patients. Four had supraclinoid aneurysms, three had sylvian aneuysms, and three had aneurysms of the anterior communicating artery. The aneurysm must be dissected out as carefully as possible and must be completely wrapped with the plastic. The plastic is a colloid, but solidifies rapidly. It must not be applied until the entire dissection has been completed.

Of 10 patients operated upon, two died. One had an aneurysm in the anterior communicating artery, after which coma developed, and hemorrhage occurred from the middle meningeal artery. The patient was cachectic and died three weeks after the operation. The second patient, who had an aneurysm of the supraclinoid portion of the carotid artery, died four days after operation from infarction of the brain.

Eight patients had good immediate results. Two of these had headaches which lasted for three weeks. Two others had aseptic meningitis which spontaneously subsided in 15 days. There were no complications related to the optic nerve, in spite of the fact that the plastic material was in contact with this nerve in some patients. There was no postoperative epilepsy or postoperative oculomotor paralysis. The longest duration of follow-up was from three months to two years.

One disadvantage of this method is that the plastic coating leaves the aneurysm in place and thereafter the aneurysm may give rise to distant embolic phenomena. The authors prefer this method to ligating the carotid artery in the neck or proximal clipping of the aneurysm.—Lapras, C. and Goutelle, A.: Le traitement des anévrysmes intra-craniens par enrobage plastique, *Neurochirurgie*, **15:** 107, 1969.

SQUAMOUS CELL CARCINOMA OF THE PREMAXILLA IN A 4-YEAR-OLD CHILD: A CASE REPORT

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Squamous cell carcinoma involving the hard and soft palate is rare. New and Hallberg[1] reported only 84 patients with this lesion in a group of 5000 with malignancy of the buccal cavity.[2] Squamous cell carcinoma involving the palate of a child is still rare although a few instances of mucoepidermoid carcinoma have been reported in children.[3, 4] In a group of 308 patients known to have palatine-arch carcinoma, none was under 20 years of age.[5]

We report one such case in a 4-year-old girl to point out that these lesions can occur in children and require specific treatment.

Clinical History

This 4-year-old girl was admitted to the Hospital for Sick Children, Toronto in September 1959, with the history of a persistent toothache in the region of the upper central incisor for three months. The family dentist attributed her symptoms to impacted deciduous teeth and the central incisors were extracted.

Within two months, the area of extraction had become a fungating, hemorrhagic lesion and roentgenograms demonstrated an associated osteolytic change in the adjacent bone with loss of the lamina dura (Fig. 1b). Three days after admission a biopsy of the lesion was taken and the pathological diagnosis was squamous cell carcinoma (Fig. 1c). After eight days, the premaxilla and the hard palate as well as the lower portion of the septum were totally resected (Fig. 2). When the packing was removed, six days after the operation, a dental model and an obturator were fabricated to act as a carrier for radon needles. This was applied a week later under general anesthesia (Fig. 3a). The obturator,

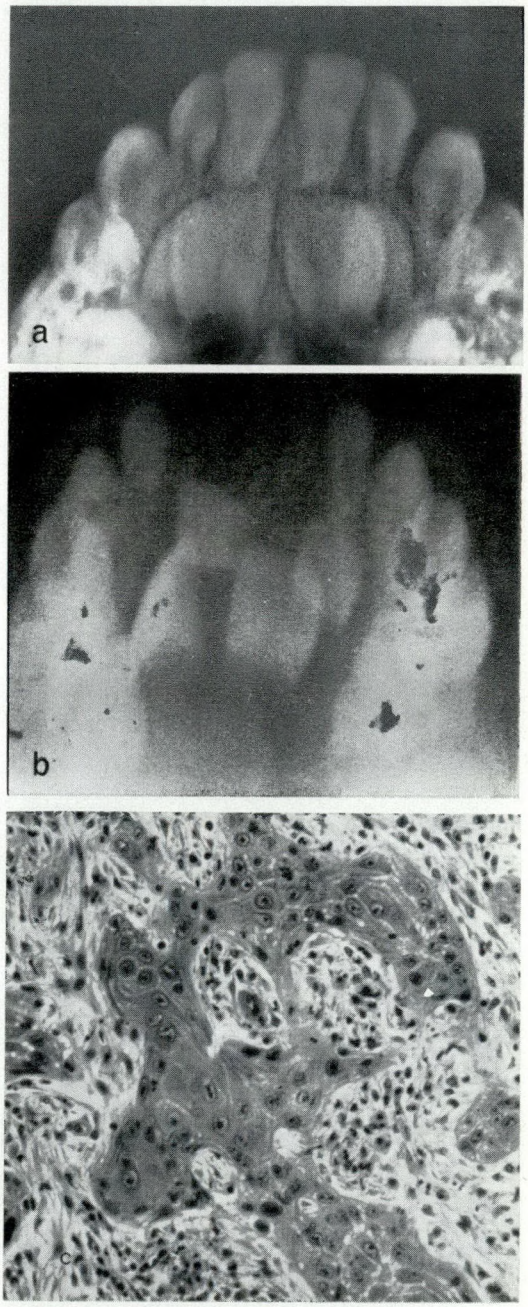

Fig. 1.—(a) Normal premaxillary radiograph in a 4-year-old child. (b) Grossly abnormal radiograph of the patient's premaxilla. (c) Photomicrograph of the squamous cell carcinoma of the premaxilla.

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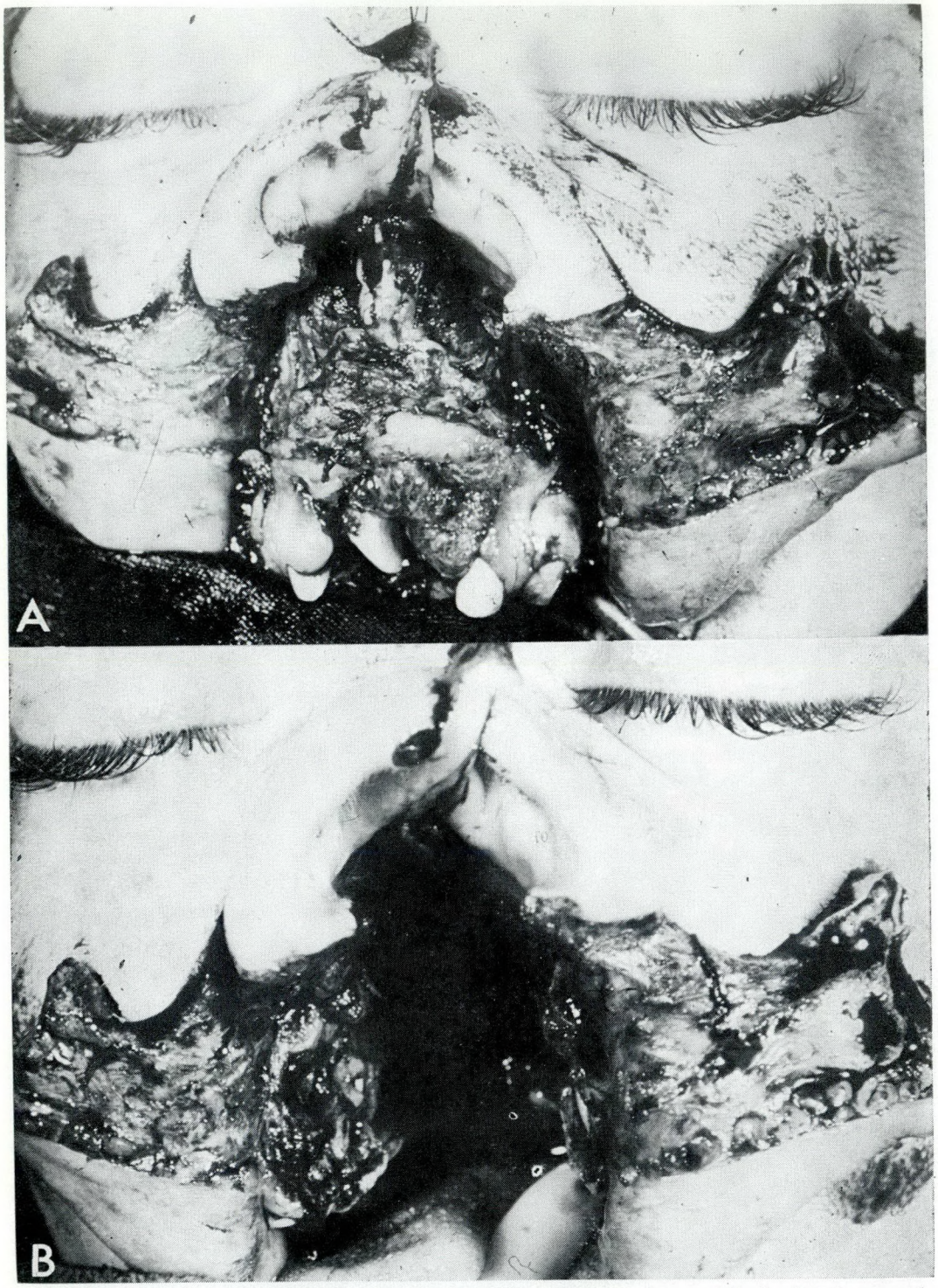

Fig. 2.—(A) Operative exposure showing the isolated tumour after a philtral-splitting approach. (B) Post-excision, with the facial flaps retracted.

loaded with radium needles, was inserted into the resection defect to give an estimated dose of 5000 R at a calculated depth of 5 mm. over a period of one week.

Fig. 3a

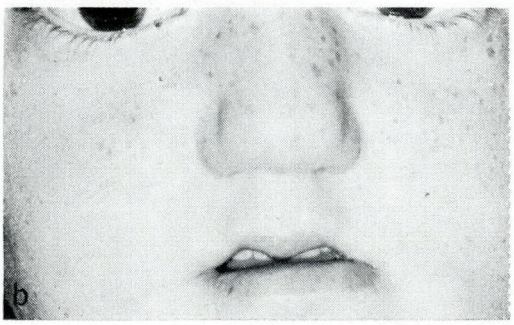

Fig. 3b

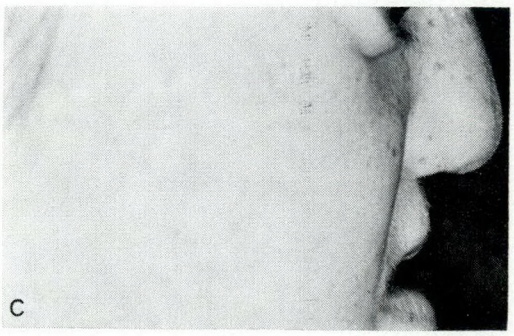

Fig. 3c

Fig. 3.—(a) Postoperative closure showing the radium prosthesis in place. (b and c) Clinical appearance of the patient four years after operation. Patient has a prosthetic denture in place.

Histopathological Examination

The diagnosis of squamous cell carcinoma had been made on the original biopsy. Cultures of the lesion revealed only *Staphylococcus aureus*, coagulase positive. Because the tumour was ulcerating and fungating, the presence of this organism was not considered significant. The available tissue was carefully searched, with appropriate stains, for any organism that might have caused a pseudoepitheliomatous hyperplasia. Senior pathologists, experienced in adult pathology, and a dental pathologist, were consulted; all agreed that such a lesion, in an adult, would be considered a squamous cell carcinoma. The microscopic appearance of the tumour, which was resected eight days after the original biopsy, was even more convincing. The proliferating epithelial cells extended deep into the tumour and there was an associated acute and subacute inflammatory reaction.

The patient was discharged from hospital five weeks after admission and reviewed in our Out-Patient Clinic at frequent intervals for one year.

The family moved away, but the patient was seen again by the authors four years after operation and there was no evidence of a local extension of her original lesion or of distant spread. A dental prosthesis subsequently fabricated to fill in the large premaxillary defect, provided a satisfactory functional and cosmetic result (Fig. 3b and c).

Discussion

Twenty-five patients with palate tumours were treated at the Hospital for Sick Children in the period 1945 to 1965. In over 2000 children with malignancy in all parts of the body, seen over the same period in this institution, this patient was the first child with squamous cell carcinoma of the palate. Rare though it is, this lesion does develop in children, and dental and medical surgeons must be aware of its existence.

Summary

A squamous cell carcinoma involving the premaxilla in a 4-year-old girl was treated by radical excision and radon needle implant for one week. She survived without complications or extension of the lesion for

at least four years, and has since been lost to follow-up.

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Résumé

Une fillette de 4 ans, souffrant d'un épithélioma spinocellulaire intéressant la région prémaxillaire, a été traitée par excision radicale et implantation d'une aiguille de radon pendant une semaine. Elle a survécu pendant quatre ans, sans complication ni propagation de la lésion, après quoi elle a été perdue de vue pour des examens ultérieurs.

REDUCTION IN SLIPPED UPPER FEMORAL EPIPHYSIS

Manipulative reduction can be performed safely in many patients with long-standing problems, even when there has been no acute episode, with little danger of ischemic necrosis. The results are at least as good as those after complicated operations that would otherwise be required.

Attempts at gradual reduction by traction have been abandoned because they are often futile and always waste valuable time. The patient is placed on an orthopedic table with the pelvis held down by an assistant; traction is applied with the hip and knee flexed 90°, and the thigh is slowly and steadily rotated medially and then abducted and finally extended. The surgeon may be firm but never forceful. Rarely does the surgeon believe that reduction has occurred.

The foot is then attached to the footpiece in abduction and medial rotation with moderate traction and roentgenograms are taken. If reduction is successful, fixation is obtained with Austin Moore pins, which are now preferred to the Smith-Petersen nail. The sooner the leg can be removed from its position of medial rotation and abduction, the better; the position menaces the blood supply to the femoral head. For the same reason, a plaster boot with a cross-bar to maintain medial rotation in bed is undesirable. The placing of the pins must ensure that there is no danger of redisplacement and the leg should be allowed to roll out.

If reduction is unsuccessful, the surgeon must resist the temptation to make another attempt. If the degree of slip is mild, tension on the leg is relaxed and the hip is pinned with the displacement uncorrected; if the degree of slip remains unacceptable, the surgeon proceeds forthwith to the further operation of his choice.

Only in mild displacement may manipulation produce only partial correction of position and this is accepted gratefully. In moderate and severe displacement, the author finds that reduction either occurs completely or not at all.

Weight bearing was avoided for at least three months. The pin or pins were removed when fusion of the epiphyseal plate neared completion, usually about a year later.

In only one patient with an acute minor slip almost perfectly reduced did growth continue. Most late roentgenograms revealed some shortening of the femoral neck, and often a little widening of the femoral head in a lateral direction with a suggestion of flattening, even though serial films had shown no suggestion of ischemic changes and the films taken imediately after reduction showed symmetric femoral heads.

The only absolute contraindication is a fused epiphyseal plate. The degree of slip and above all the duration of symptoms should not preclude an attempt at manipulative reduction. Of the 16 hips treated by manipulative reduction, conditions in four were acute, with two weeks' premonitory symptoms in two of them. In all but one of these four, the slip was almost complete. Reduction performed in each instance within 72 hours was apparently perfect, one being over-reduced at first.—Fairbanks, T. J.: Manipulative reduction in slipped upper femoral epiphysis, *J. Bone Joint Surg.* [*Brit.*], **51B:** 252, 1969.

CONGENITAL ABSENCE OF THE PERICARDIUM: A CASE REPORT*

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ALTHOUGH congenital defects of the pericardium have long been recognized, only 116 cases have been reported since the initial description by Columbus[1] over 400 years ago. Two types of defect have been described: complete absence of the pericardium on one side of the heart, and partial or foramen-type defects. The purpose of this paper is to describe a patient with congenital total absence of the left pericardium and to emphasize certain aspects of the diagnosis and the possible clinical significance of this anomaly.

CASE REPORT

Miss C.S., a 22-year-old woman, was first admitted in May 1965 after a routine physical examination had disclosed a heart murmur. Her complaints, which were minimal, consisted of slight shortness of breath on exertion, fatigue, and infrequent vague chest pains. Functional inquiry was negative except for frequent headaches; the patient's previous health had been excellent. This apparently healthy young woman had no evidence of cyanosis and pulses were physiological throughout. Her blood pressure was 113/73 mm. Hg. The apical pulse was within the midclavicular line and there was no evidence of right ventricular hypertrophy. On auscultation first and second sounds were normal throughout and the second sound varied normally with respiration. A faint systolic murmur, which was loud on inspiration and disappeared on expiration, was heard at the apex and also below the tip of the left scapula. The remainder of the examination was unremarkable. Her hemogram and urinalysis were normal. The electrocardiogram revealed right axis deviation but no other abnormality. On cardiac fluoroscopy, she had a small vertical heart with a somewhat prominent main pulmonary artery segment (Fig. 1). By ear oximetry, oxygen saturation at rest was 97% and 98%.

The patient was discharged without a definite diagnosis but was admitted again two years later, in June 1967, for further investigation. Again she had no complaints except for occasional momentary pains radiating around the left costal margin, not related to activity or posture. On this occasion she had a continuous murmur, which almost disappeared on expiration, at the apex and below the tip of the left scapula, and visible pulsations in the fifth left interspace at the anterior axillary line. Her electrocardiogram and fluoroscopy were repeated and, in addition, a thoracic aortogram was performed, but we could not demonstrate any anomaly of the cardiovascular system.

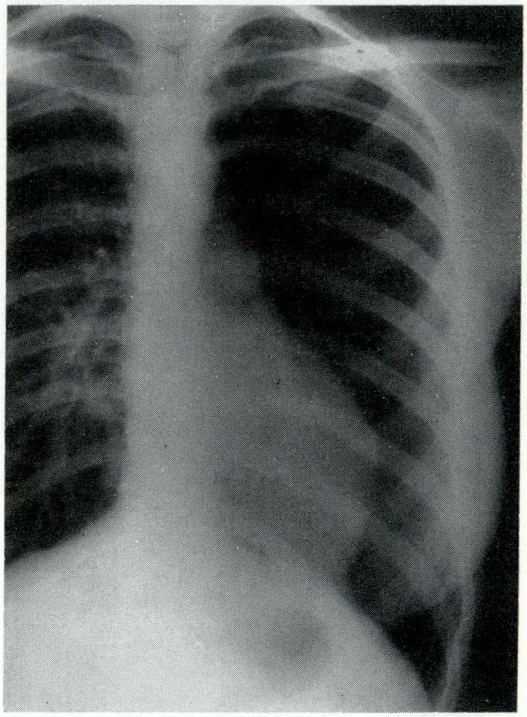

Fig. 1.—Preoperative chest roentgenogram showing prominence of the pulmonary artery segment and slight shift of the heart shadow to the left.

In order to exclude an intercostal artery aneurysm or possible arteriovenous malformation, a left thoracotomy was done. The left intercostal arteries were small and normal but, on entering the left pleural space, we saw the left atrium and ventricle immediately—there was no left pericardial sac. She had no other cardiac anomaly and hence the thoracotomy was closed. The patient's recovery was uneventful and complete.

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Discussion

Columbus[1] described a patient with pericardial deficit in 1559. However, the first verified case of congenital absence of the pericardium was reported by Baillie[2] in 1793. Since then there have been random reports of the condition in man and other mammals;[3-5] in all, 116 cases have been reported in man. The anomaly can be classified into right-sided and left-sided defects and further subdivided into large or complete defects, and small or foramen-type defects. Most pericardial defects occur on the left side and, of these, a complete absence of the pericardium is far more common than a foramen-type defect.[6] Right-sided defects are extremely rare.

Etiology

Although the normal embryology of the region is well described, the etiology of the condition remains obscure. Most authors agree that pericardial defects probably represent faulty development of the pleuropericardium, but they differ about the cause of this fault. Several[7, 8] have suggested that a normal lung bud herniates through the pleuropericardial foramen and prevents its closure. Risel[9] suggested that this absence represents primary atresia of the pleuropericardial membrane and failure of the lung roots to join. McGarry[10] postulated that rotation of the developing liver traumatized the ridge from which the membrane develops. The most widely accepted theory, that of Perna[11] and Plaut,[12] proposes that the premature atrophy of the left duct of Cuvier reduces the blood supply to the pleuropericardial membrane. This explanation accounts for the preponderance of left-sided defects.

Clinical Features

The clinical features of congenital pericardial absence are variable; this anomaly is usually benign, and less than one-fifth of the recorded cases were recognized before death. In the more common complete absence of the left pericardium, there is no disturbance of cardiac function; it is this type of defect which is recognized most widely in the living patient as an incidental finding at thoracotomy. The partial, foramen-type defect, although infrequent, may prove to be life-threatening if the heart herniates and strangulates through the defect.[13, 14]

Symptoms

Most patients with large or complete pericardial defects have no symptoms. Some complain of transient chest pain or shortness of breath with change in posture —symptoms which may be due to tension on the commonly found cardiopleural adhesions. Because the pericardium is absent chest pain may also be due to increased stress on the anchoring structures of the cardiac base or to intermittent compression of the left coronary artery by the margin of a pericardial defect.

Physical Findings

Physical findings are also variable. A variety of systolic murmurs has been described and these, when present, may be due to turbulence set up at the base of an unusually mobile heart. When the left pericardium is deficient the apical impulse may be shifted to the left. Often no unusual physical findings are reported with the uncomplicated foramen-type defect.

Diagnosis

In partial pericardial defects without herniation, there may be no demonstrable abnormality on the chest film. Protrusion of the heart through a foramen may produce an abnormal prominence in the area of the left pulmonary artery which represents a herniated left atrial appendage. In complete absence of the left pericardium, the heart and aortic knob are usually displaced to the left; the left heart border is flattened and the pulmonary artery segment is unusually long and well defined. In the diagnosis of pericardial defects, diagnostic pneumothorax is the procedure of choice. In 1937 Dahl,[15] when he identified gas in the left pericardium in a patient in whom he had created a left pneumothorax to treat tuberculosis, made a correct diagnosis of pericardial deficit. In 13 patients (out of a total of 116) the diagnosis of congenital pericardial defect has been established by means of artificial pneumo-

thorax, i.e. without operation. Although this procedure may fail when the patient has pleuropericardial adhesions, this has not yet been described.

Angiocardiography contributes to the diagnosis of partial defects in which a portion of the heart herniates but not when the entire left or right pericardium is absent or when there is no herniation. Cardiac catheterization has been of value only in excluding other cardiac abnormalities. The electrocardiogram may show marked changes in the electrical axis of the QRS complexes if the heart is not in its normal intrathoracic position.

Up to 30% of these patients have had associated anomalies such as patent ductus arteriosus (15 patients), tetralogy of Fallot (two), bronchial insufficiency (six), bifid apex of heart, bicuspid aortic valve, tricuspid insufficiency, aberrant pulmonary lobes and others. For this reason, every patient with pericardial deficit should be thoroughly investigated.

Asymptomatic patients with pericardial defects need no specific treatment. However, Fosburg, Jakubiak and Delaney[16] stressed that foramen-type defects have a lethal potential and advocated prophylactic repair. Various authors recommended that the defect be closed with pleural flaps or prosthetic materials, or that plastic procedures be done on the pericardium. Pericardiotomy, although offered as a treatment, does not prevent cardiac torsion or displacement and does not isolate the heart from the pleural space. In any event, when pericardial defects are diagnosed the likely prognosis should dictate their treatment.

Summary

A 24-year-old woman had congenital absence of the left pericardium. The defect was discovered at thoracotomy after thorough investigation of a systolic murmur had not disclosed identifiable disease.

Congenital absence of the pericardium, a rare anomaly, is most often diagnosed at operation. Most of these patients have a complete absence of the left pericardium; a minority have partial or foramen-type defects. Patients with large left pericardial defects usually have no symptoms and are investigated because of a variety of systolic murmurs. These defects are benign and require no treatment. Small pericardial defects, however, may kill the patient if the heart herniates through the foramen and strangulates. Because of this complication and the frequent association of pericardial defects with other cardiac and pulmonary anomalies, every such patient should receive thorough investigation. The diagnosis of pericardial absence can be established without thoracotomy if a left pneumothorax is done. The size and symptoms associated with the pericardial defect dictate the treatment. Operative closure of the defect is necessary in only a small number.

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Résumé

Les auteurs présentent le cas d'une femme de 24 ans sou souffrant d'une absence congénitale du péricarde gauche. Cette anomalie a été découverte à la thoracotomie, pratiquée après un examen complet qui n'avait pas permis d'identifier la nature d'un souffle systolique.

L'absence congénitale du péricarde est une anomalie rare qu'on ne découvre la plupart du temps qu'au moment d'une opération. Chez la majorité des malades, l'absence du péricarde gauche est complète, les autres cas se présentant sous la forme d'aplasie partielle ou fenestrée. Les malades dont les anomalies péricardiennes sont considérables ne présentent habituellement aucun symptôme et ils sont examinés pour découvrir la cause de divers souffles systoliques. Ces derniers sont bénins et n'exigent pas de traitement. Par contre, les défauts de petite dimension peuvent avoir une issue fatale par herniation et étranglement du cœur à travers l'orifice. Cette complication, outre le fait que les défauts du péricarde s'accompagnent souvent d'autres pathologies cardio-pulmonaires, impose une grande vigilance devant tout cas de l'espèce. En dehors de la thoracotomie, on peut poser un diagnostic d'absence du péricarde par un pneumothorax gauche. Selon les dimensions de l'orifice et les symptômes existants, le chirurgien pourra décider lesquels, parmi le petit nombre de patients dont l'anomalie comporte un risque mortel, devront subir la fermeture chirurgicale de l'orifice.

CYTOSTATIC DRUGS IN TREATMENT OF TROPHOBLASTIC NEOPLASIA

In the past six years the authors have observed 42 patients who had hydatidiform mole and 52 who had invasive trophoblastic disease. The arbitrary classification included simple mole, without any evidence of hyperplasia or anaplasia of the trophoblast; simple mole extending through the myometrium; destructive mole; and chorionepithelioma, which is synonymous with choriocarcinoma. The series was studied and the effects of the cytostatic drugs reported.

In addition to the morphologic bases for the diagnosis, clinical, radiologic, and hormonal evaluations were used to classify these tumours. Quantification of urinary gonadotrophin titers and follow-up studies at least once a week were used to evaluate the day-to-day effects of the treatment. The authors believe that molar pregnancy should be suspected if a positive result is obtained by dilution over 1:500 in the second month, 1:1000 in the third month, 1:500 in the fourth to fifth month. Further detection under the base-line titer depends on bioassay when immunologic determination in undiluted urine is negative. The drugs used included dactinomycin and vinblastine sulfate as well as thiotepa, cyclophosphamide, mitomycin C, and chromomycin A_3.

In recent years methotrexate has been used exclusively unless there was known pre-existing renal, hepatic, and hematopoietic impairment. If, during the course of the drug, the white blood cell count fell below 3000/c.mm., or the platelet count below 100,000/c.mm., the drug was suspended and resumption of treatment was delayed for a time. Three identical courses were given after a lapse of approximately 14 days from the initial course.

All patients were followed monthly for six months, bi-monthly for the next six months, four times a year for the next year and twice a year thereafter.

Forty-two women with hydatidiform mole were treated by evacuation during the six-year period. Four of them showed subsequent persistence of urinary gonadotrophin five weeks after evacuation. A definite diagnosis of chorionepithelioma was made in 13 patients over the same period.

The authors state that in their experience a patient with metastatic chorionepithelioma seldom survived. If survival is possible, the diagnosis is probably benign. None of the 13 patients who have attained remission in this series was diagnosed as having chorionepithelioma.

The authors disagree with those who advocate methotrexate instead of hysterectomy, and believe that hysterectomy may suffice where the disease is limited to the uterus. They note that the procedure yields an accurate diagnosis and sometimes induces spontaneous resolution of the secondary lesions. However, none of their 13 patients with chorionepithelioma was successfully treated.—Akasu, F., Honma, J. and Minami, M.: Use of cytostatic drugs in treatment of trophoblastic neoplasia, *Acta Obstet. Gynec. Japonica*, **16:** 108, 1969.

FIBROME DU BASSINET*

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Le but de ce travail est de présenter un cas de tumeur du bassinet à cause de sa rareté et de sa structure particulière. Après un bref exposé de l'histoire clinique de la malade et de l'aspect pathologique de la lésion, nous discuterons de la fréquence d'une telle tumeur et de son appellation.

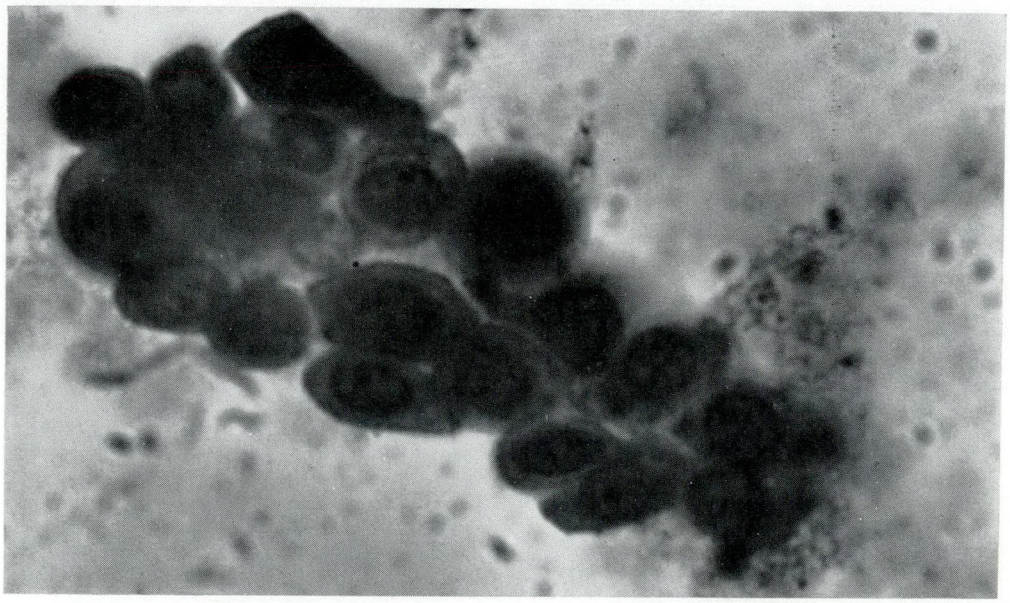

Fig. 1.—Cytologie des urines. Groupe de cellules transitionnelles montrant quelques noyaux denses (coloration de Papanicolaou × 400).

Observations

Mme N.D., 42 ans, mère de quatre enfants en excellente santé, consulte à l'Hôtel-Dieu de Québec le 31 août 1966 pour troubles urinaires depuis un mois et demi manifestés par de la pollakiurie, de la nycturie et des brûlements à la miction. La patiente raconte avoir fait une hématurie non douloureuse qui a duré deux jours avec passage d'un caillot allongé en forme de spaghetti. A l'examen de l'abdomen, on provoque une douleur à la palpation du flanc droit et de la fosse iliaque droite. Dans les antécédents de la malade, il n'y a rien de contributoire sauf une discoïdectomie sept ans auparavant. Les épreuves biologiques sont dans la limite de la normale.

Un examen cytologique pratiqué sur du matériel de lavage du bassinet au sérum physiologique montre quelques groupes de cellules transitionnelles disposées à la façon de fragments tissulaires, faisait soupçonner la présence d'une lésion tumorale de nature épithéliale (Fig, 1). En présence de ce matériel cytologique, il était difficile de déterminer la nature bénigne ou maligne de la tumeur et nous avons préféré classer cet échantillon comme suspect vu la présence de quelques atypies nucléaires.

L'urographie intra-veineuse met en évidence au niveau du bassinet du rein droit, une image lacunaire à contours festonnés s'étendant de la base des calices supérieurs jusqu'à la jonction urétéro-pyélique (Fig. 2). La présence d'une lésion tumorale du bassinet droit est alors diagnostiquée. Pour préciser la nature de la tumeur, on procède à une pyélographie rétrograde afin de mieux délimiter la lésion (Fig. 3). Une cystoscopie permet également d'éliminer une tumeur vésicale.

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*Travail présenté au congrès de l'Association des Médecins de laboratoire de la Province de Québec tenu au Mont Gabriel Lodge, Qué., les 12 et 13 septembre, 1968.

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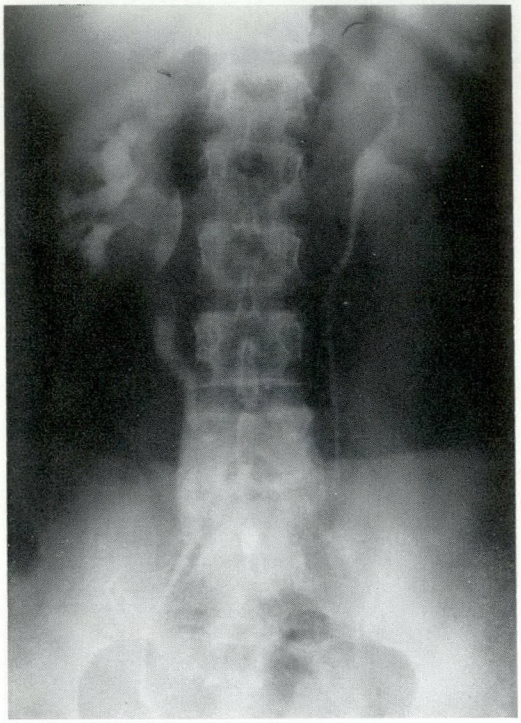

Fig. 2.—Urographie intraveineuse. Défaut de remplissage de la partie supérieure du bassinet droit et d'un segment supérieur de l'uretère.

Fig. 3.—Pyélographie rétrograde. Image confirmant la présence d'une tumeur à la partie supérieure du bassinet.

Le diagnostic de tumeur du bassinet étant posé, on procède à une lombotomie suivie d'une pyélotomie. A l'ouverture du bassinet, la tumeur de consistance mollasse et de coloration blanc-rosée fait hernie dans la plaie. Elle est attachée à la paroi antéro-supérieure du bassinet par un mince pédicule de 0.5 cm de diamètre. La tumeur est réséquée sur son pédicule et comme un examen extemporané élimine la possibilité d'une tumeur maligne, on procède à la fermeture du bassinet en ayant soin d'électrocoaguler le pédicule restant. Les suites opératoires sont excellentes et la malade est libérée après 17 jours d'hospitalisation.

L'examen de la pièce au laboratoire consiste en un fragment de tissu de 4 x 4 x 2 cm formé de nombreuses franges dont la surface est blanchâtre avec parfois un piqueté hémorragique. Le tissu de ces franges est très mollasse, d'aspect gélatineux. Sur l'une des faces, on retrouve une zone anfractueuse correspondant au point d'implantation de la masse tumorale. A l'examen microscopique, la tumeur présente de nombreux axes formés d'un tissue fibreux très œdématié et lâche d'aspect myxomateux. Ce tissu est généralement peu cellulaire, richement vascularisé et contient ici et là d'assez nombreux lymphocytes et plasmocytes (Fig. 4). Cette tumeur est recouverte par un épithélium de type urinaire qui est généralement mince avec quelques foyers d'hyperplasie où les cellules sont généralement régulières (Fig. 5). Il n'y a aucun signe de malignité. Le diagnostic final est donc celui de fibrome lâche papillaire du bassinet.

Discussion

Les tumeurs bénignes du bassinet sont d'une extrême rareté si l'on exclut certaines tumeurs bénignes du rein comme les adénomes ou fibro-adénomes qui font hernie dans la partie supérieure des voies excrétrices du rein et certaines tumeurs de l'épithélium du bassinet qui sont considérées comme des papillomes ou des épithélioma papillaires grade I.[1-4] La tumeur bénigne d'origine mésenchymateuse prenant naissance de la paroi du bassinet représente un infime pourcentage des lésions que l'on retrouve tant dans notre matériel chirurgical qu'autopsique. Certains auteurs n'en font pas mention dans

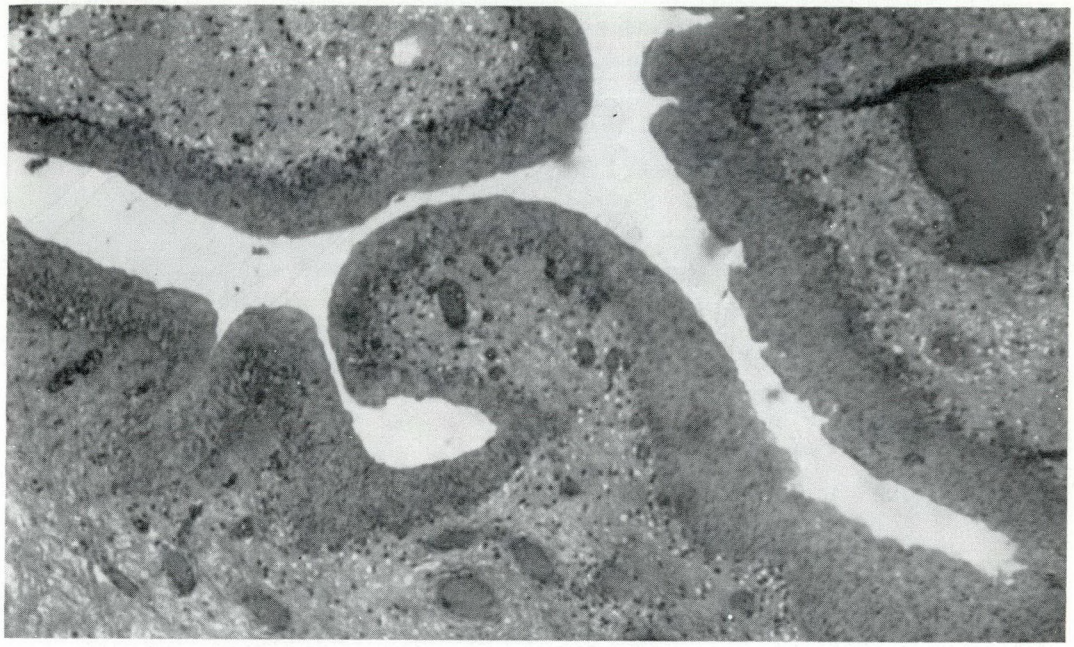

Fig. 4.—Fragment de tumeur montrant son aspect papillaire et sa composante conjonctive lâche, riche en vaisseaux (H & E × 40).

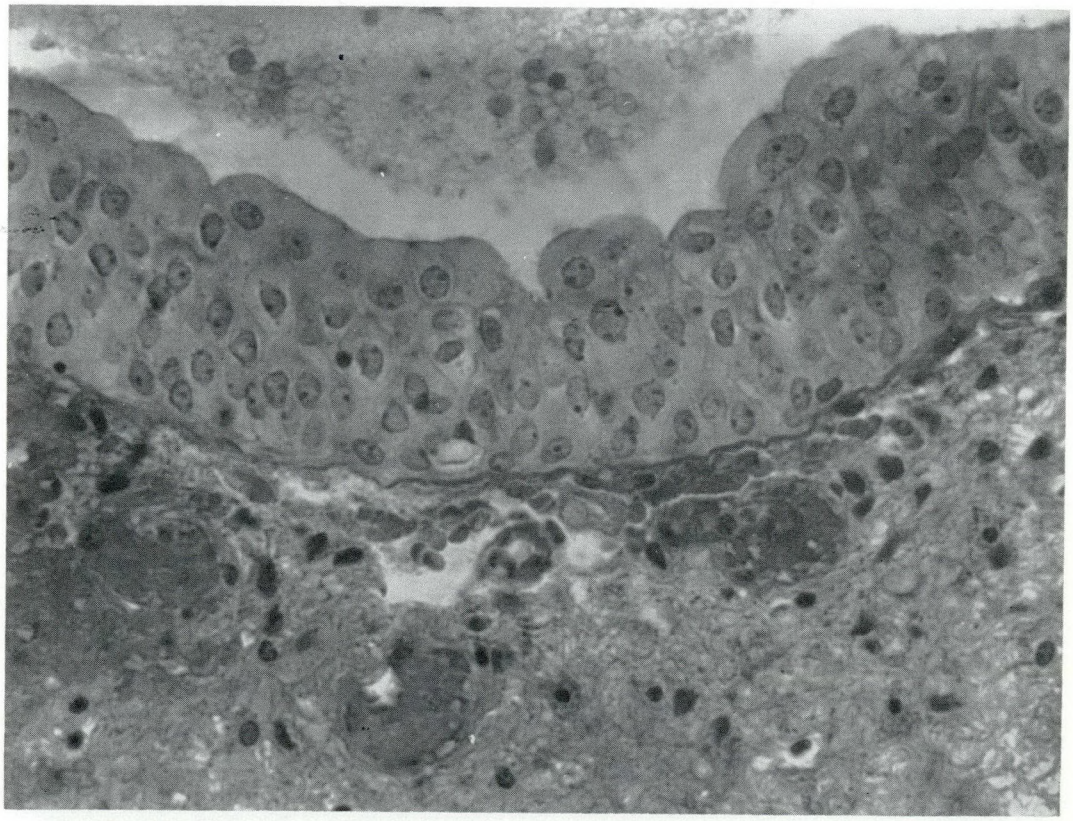

Fig. 5.—L'épithélium de revêtement est de type transitionnel et régulier (H & E × 250).

leurs publications concernant les tumeurs des voies urinaires. En relevant la littérature, nous avons retracé une publication hongroise de 1929, où les auteurs rapportaient un cas identique. En 1951, un second cas fut rapporté aux Etats-Unis[5] et en 1957, Lucke et Schlumberger[6] dans l'atlas des tumeurs du rein, du bassinet et de l'uretère de l'institut de Pathologie des Forces Armées Américaines n'en relevèrent que deux cas. En 1963, Shucksmith[7] publia un nouveau cas de fibrome du bassinet et à son avis, il représenterait le troisième cas de la littérature. Les tumeurs rapportées par ces différents auteurs comme fibromes du bassinet semblent correspondre assez bien à celle que nous avons retrouvée chez notre patiente, si l'on tient compte de sa composante conjonctive, de sa localisation et de son évolution favorable. Nous croyons que ce cas pourrait être le quatrième à être rapporté bien que nous n'avons pas la prétention d'avoir épuisé la littérature médicale et que nous sommes convaincus qu'il existe d'autres cas qui n'ont pas été publiés.

Un autre point que nous croyons important d'aborder en face d'une telle tumeur, c'est celui de son appellation. Le terme fibrome signifie une tumeur bénigne à point de départ du tissu conjonctif.[8] La tumeur de notre patiente se compose en très grande partie de tissu conjonctif qui prend des aspects variables dus à sa configuration et à sa localisation. L'œdème, l'abondance des vaisseaux et les foyers d'infiltrat inflammatoire chronique représentent des signes de souffrance tissulaire avec phénomènes de réparation tels que rencontrés dans certaines tumeurs pédiculées de l'utérus ou de l'intestin. L'épithélium de surface ne semble pas faire partie de la tumeur comme telle mais simplement la recouvrir à la façon de la muqueuse gastrique qui est refoulée par un léiomyome sous-muqueux. Ce qui semble le plus paradoxal pour cette tumeur bénigne mésenchymateuse, c'est l'absence de limite précise et de capsule. Cette tumeur présente un pédicule comme un polype intestinal et sa surface est formée de multiples franges.[9, 10] Au point de vue histogénèse, nous croyons que cette lésion pourrait se rapprocher des tumeurs inflammatoires rapportées à l'estomac[11] et à l'intestin où l'on est en face de lésions tumorales sans limite précise et possédant une composante surtout conjonctive accompagnée de nombreux vaisseaux et de cellules inflammatoires. A cause de l'absence de musculaire muqueuse et de sous-muqueuse propre au niveau des voies excrétrices de l'arbre urinaire, une telle tumeur peut prendre un aspect différent de celle du tube digestif en devenant pédiculée et frangée.

En résumé, nous avons présenté le cas d'une tumeur bénigne du bassinet, connue sous le nom de fibrome survenu chez une patiente de 42 ans. Après avoir exposé l'aspect macroscopique et microscopique de cette lésion, nous avons cru opportun de discuter de sa rareté et de son appellation.

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Summary

A benign tumour of the renal pelvis, a fibroma, was resected in a 42-year-old woman without incident.

We have discussed the gross and microscopic aspects of this rare lesion for which the name fibroma is more or less suitable.

This is presumably the fourth case in the literature.

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Manuscripts in duplicate of original articles, case reports, and other contributions should be forwarded with a covering letter requesting consideration for publication in *The Canadian Journal of Surgery*. Acceptance is subject to the understanding that they are submitted solely to this Journal, and will not be reprinted without the consent of the author and the publishers. Acceptance or rejection of contributions will be determined by the Editorial Board. As space is available, a limited number of case reports will be published. Articles should be typed on one side only of unruled paper, double-spaced, and with wide margins. The author should always retain a carbon copy of material submitted. Every article should contain a summary of the contents. The Concise Oxford Dictionary will be followed for spelling. Dorland's Illustrated Medical Dictionary will be followed for scientific terminology. The Editorial Board reserves the right to make the usual editorial changes in manuscripts, including such changes as are necessary to ensure correctness of grammar and spelling, clarification of obscurities or conformity with the style of *The Canadian Journal of Surgery*. In no case will major changes be made without prior consultation with the author. Authors will receive galley proofs of articles before publication, and are asked to confine alterations of such proofs to a minimum.

Reprints

Reprints may be ordered on a form which will be supplied with galley proofs. It is important to order these before publication of the article, otherwise an extra charge for additional type-setting will be made.

References

References should be referred to by numerals in the text. They should include in order: the author's name and initials in capitals, title of the article, abbreviated journal name, volume number, page number and year. The abbreviations of journal names should be those used by the National Library of Medicine, Washington, D.C., as published in *Index Medicus*. References to books should include in order: author's name and initials, title of book, number of edition (e.g. 2nd ed.), title of publishing house, city of publication, year of publication, page number if a specific reference.

Illustrations

A reasonable number of black-and-white illustrations will be reproduced free with the articles. Colour work can be published only at the author's expense. Photographs should be glossy prints, unmounted and untrimmed, preferably not larger than 10″ x 8″. Prints of radiographs are required and *not the originals*. The magnification of photomicrographs must always be given. Photographs must not be written on or typed on. An identifying legend may be attached to the back. Patients must not be recognizable in illustrations, unless the written consent of the subject for publication has been obtained. Graphs and diagrams should be drawn in India ink on suitable white paper. Lettering should be sufficiently large that after reduction to fit the size of the Journal page it can still be read. Legends to all illustrations should be typed separately from the text and submitted on a separate sheet of paper. Illustrations should not be rolled or folded.

Language

It should be clearly understood that contributors are at full liberty to submit articles in either English or French, as they please. Acceptance will be quite independent of the language of submission. If the contributor wishes, he may submit an informative summary of not more than 300 words in the language other than that in which he has submitted the article. For example, an article in English must carry an English summary and may, if the author wishes, carry a more detailed summary in French.

LE JOURNAL CANADIEN DE CHIRURGIE

Toute communication concernant le Journal devra porter la mention "Le journal canadien de chirurgie" et être adressée à l'Editeur, Publications de l'A.M.C., 129 Adelaide Street West, Toronto.

Le journal est publié trimestriellement. Le prix de l'abonnement est de $10. par an ($5. par an pour les médecins qui sont résidents en chirurgie) et commence avec le numéro de janvier de chaque année. Un exemplaire isolé coûte $2.50 et est payable d'avance. (Nous serions reconnaissants aux souscripteurs de vouloir bien ajouter à leur chèque le montant des frais bancaires éventuels).

INSTRUCTIONS A NOS COLLABORATEURS

Manuscrits

Les manuscrits d'articles originaux, de rapports cliniques etc. seront envoyés en deux exemplaires, accompagnés d'une lettre demandant qu'on veuille bien considérer leur publication dans ***Le journal canadien de chirurgie.*** Ils ne seront acceptés qu'à la condition qu'ils n'aient été soumis qu'à notre Journal et qu'ils ne soient pas réimprimés sans le consentement exprès de l'éditeur et l'auteur. L'acceptation ou le refus des articles soumis relève du Conseil de la publication. Si la place est disponible, un nombre limité d'histoires cliniques pourront être publiés. Les articles seront dactylographiés sur un seul côté d'un papier non ligné, à double espace et avec une large marge. L'auteur devra toujours conserver une copie au papier carbone du texte soumis. Tout article devra être accompagné d'un résumé. L'orthographe sera celle adoptée par le dictionnaire Larousse. Quant à la terminologie scientifique, elle sera basée sur le Dictionnaire des termes techniques de médecine ou tout autre ouvrage de référence sérieux. Le Conseil de la publication se réserve le droit d'apporter au texte les changements qu'il jugerait à propos pour assurer la correction grammaticale et l'orthographe, pour éliminer d'éventuelles obscurités ou pour rendre la présentation conforme au style du *Journal canadien de chirurgie.* Aucun changement important ne sera apporté au texte sans que l'auteur aît été préalablement consulté. Les auteurs recevront avant la publication des épreuves d'imprimerie de leur texte, auxquelles ils sont priés d'apporter le minimum de corrections.

Tirés-à-part

On pourra commander des tirés-à-part sur une formule qui est envoyée avec les épreuves. Il est important de les commander avant la publication de l'article, sous peine de devoir payer un supplément pour une nouvelle composition.

Bibliographie

Les références bibliographiques seront indiquées par des numéros dans le corps du texte. Elles comprendront dans l'ordre: le nom de l'auteur et ses initiales, en majuscules, le titre abrégé du Journal, le numéro du volume, le numéro de la page et l'année. Les abréviations admises pour les noms de revues sont celles qui figurent dans *l'Index Medicus* de la Bibliothèque Nationale de Médecine, Washington, D.C. Les renvois aux livres comprendront dans l'ordre: le nom de l'auteur, ses initiales, le titre de l'ouvrage, le numéro de l'édition (p. ex. 2ème éd.), le nom de la maison d'édition, la ville où elle est située et l'année de la publication; enfin, le numéro de la page s'il s'agit d'un renvoi précis.

Illustrations

Le journal accepte de publier gratuitement un nombre raisonnable d'illustrations en noir et blanc. Les reproductions de clichés en couleurs seront publiées aux frais de l'auteur. Les photographies seront imprimées sur papier brillant, ne seront ni montées ni calibrées et d'un format maximum de 8" x 10". En ce qui concerne les radiographies, nous demandons des copies et *non pas l'original.* On devra toujours fournir un agrandissement de microphotographies. Il ne faut jamais écrire ou dactylographier un texte quelconque sur les photographies. Une légende les identifiant pourra être jointe au dos. Dans les illustrations montrant des malades, ceux-ci ne pourront être reconnus, à moins qu'ils n'en aient donné le consentement écrit préalablement à la publication. Les graphiques et diagrammes seront dessinés à l'encre de Chine sur un bon papier à dessin blanc. Le lettrage devra être écrit en caractères assez grands pour que, après réduction proportionnelle au format du Journal, ils soient encore lisibles. Les légendes devant accompagner les illustrations seront dactylographiées sur une feuille indépendante du texte. Les illustrations ne seront ni roulées ni pliées.

Langue véhiculaire

Il doit être clairement établi que les collaborateurs ont pleine liberté de soumettre leurs articles en français ou en anglais, à leur choix. L'acceptation de l'article sera entièrement indépendante de la langue choisie par l'auteur. Si le collaborateur le désire, il peut décrire le contenu de l'article en un sommaire ne dépassant pas 300 mots et dans une langue différente de la langue choisie pour l'article lui-même. Par exemple, un article écrit en français doit comporter un résumé en français et peut, si l'auteur le désire, être accompagné d'un sommaire plus détaillé en anglais.

BOOK REVIEWS

AFTER VAGOTOMY. Edited by J. Alexander Williams and Alan G. Cox. 433 pp. Illust. Butterworth & Co. (Publishers) Ltd., London; Butterworth & Co. (Canada) Ltd., Toronto, 1969. $18.25.

This book draws the reader's attention to the many influences that vagal nerves exert upon the stomach and other parts of the intestinal tract.

The first section considers the pathophysiology of vagotomy as it affects the esophagus, stomach, biliary tract, pancreas and small intestine, and outlines the risk of vagal regeneration and precautions taken to prevent this.

In the second section the results of vagotomy are assessed by comparing results of the different operations, by reviewing the clinical results and considering the effects of vagotomy on nutrition, digestion and absorption, hematopoiesis and bone metabolism.

Section three covers the major complications of vagotomy—gastric retention, recurrent ulceration, diarrhea and the unsatisfied patient. Here possible prevention and correction of these problems are well analyzed.

The practical problems associated with vagotomy are considered in section four. Here the authors conclude that before we can determine the value of gastric secretion tests in the selection of the ideal procedure for each individual ulcer patient we need further knowledge of the acid-pepsin role in duodenal ulceration and recurrent ulceration after vagotomy. The techniques for achieving a complete vagotomy, performing a selective vagotomy and a properly functioning drainage procedure are described. The important role of antrectomy with vagotomy in patients with severe duodenal ulcer diathesis is emphasized. The controversies between the proponents of postoperative gastric tubes and their opponents, and the relative merits of different tubes are discussed in this section. The radiologist's difficulty in distinguishing between recurrent ulceration and deformity secondary to pyloroplasty is also considered.

Special emergency indications for vagotomy and drainage include bleeding and perforation of a duodenal ulcer where this procedure appears to be safe and corrective. The use of vagotomy and pyloroplasty to treat gastric ulcer or hiatus hernia not associated with duodenal ulceration must remain suspect at this time.

In the final chapter, the editors discuss problems which concern all surgeons with a major interest in gastroduodenal surgery: (a) After vagotomy, how do patients fare? (b) What is the best operation for peptic ulcer? (c) What are likely to be the important future developments?

This book will educate gastric surgeons about vagotomy and its many manifestations and stimulate them to think of future possible improvement in the management of duodenal ulceration.

CHEMOTHERAPY OF CANCER. Edited by Warren H. Cole. 349 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1970. $13.75.

This multi-authored book provides contemporary information on the drugs used to treat cancer. The authors were chosen because of their vast experience in their assigned subjects. As usual in such joint ventures, there is much needless repetition and inconsistency of organization. Many of the authors have provided convenient summarizing tables and impressive bibliographies.

The opening chapter on the mechanism of action of anti-cancer drugs describes its subject with much detail (almost too much for the average reader). The succeeding chapters report the empirical experiences with the agents used in the leukemias and lymphomas, the solid tumours, hormonal therapy, regional perfusion, regional intra-arterial infusion, Wilm's tumour and adjuvant chemotherapy.

For surgeons the best part of the book is Robert W. Talley's model chapter on systemic chemotherapy of human malignant neoplasms. Clear tables summarize the informative text which includes general as well as specific data on all aspects of the non-hormonal anti-cancer drugs. Surgeons will also appreciate the technical details in the chapters on regional perfusion and infusion. Unfortunately the chapter on adjuvant therapy is divided into six sections written by four different groups of sometimes over-sanguine authors.

The book should be in all institutional libraries for reference by those treating, or learning to treat cancer patients. It is too specialized for individual clinicians other than medical oncologists.

CARDIOVASCULAR SURGERY. Current Practice. Vol. 1. Edited by Thomas H. Burford and Thomas B. Ferguson. 273 pp. Illust. The C. V. Mosby Company, St. Louis, 1969. $19.80.

This volume deals only with selected topics in cardiac surgery, but these constitute the most important areas currently challenging experimental and clinical research in this field. The topics include: extracorporeal circulation, general and respiratory postoperative care of open heart patients, valvular heart surgery using prosthetic, homologous and heterologous grafts, myocardial revascularization, cardiac

transplantation and ventricular assist devices. This text, therefore, is not intended to provide complete and comprehensive coverage of the whole of cardiac and vascular surgery. It is primarily of interest to cardiac surgeons and should not, as Lord Brock suggests in the foreword, be recommended to "all surgeons of whatever specialty".

Each chapter has been written by an authority who has previously made contributions to the knowledge in the particular aspect which he discusses in this text. In each instance, the discussion is in the nature of a collective review. These evaluations are clear, factual and unbiased. Where pertinent, historical facts have been included and the direction in which research and clinical work is headed has been indicated.

A chapter on the tetralogy of Fallot, although written with clarity and authority and providing an up-to-date review of this lesion, seems out of place in this particular volume because it falls into a different category from the other subjects covered. Operation for tetralogy of Fallot is not controversial and, since the book is obviously not meant to cover the breadth of cardiovascular surgery, this topic belongs in a volume that deals with individual congenital and acquired heart lesions about which there is more uniform agreement and where great strides in research and treatment are less likely.

This book is an excellent review of the pertinent, timely, controversial and important problems in cardiac surgery today. While it is meant for surgeons with highly specialized interests, it will serve well as a reference for others who wish to review the status of these aspects of cardiac surgery in 1969.

CURRENT TOPICS IN SURGICAL RESEARCH. Second Annual Meeting of the Association for Academic Surgery, held at Washington University School of Medicine, November, 1968. Vol. 1. Edited by George D. Zuidema and David B. Skinner. 518 pp. Illust. Academic Press, Inc., New York, 1969. $21.00.

"Current Topics in Surgical Research", the proceedings of the Second Annual Meeting of the Association for Academic Surgery, which was held at Washington University School of Medicine, November 1968, contains 44 papers by these "young Turks" on the following subjects: transplantation, oncology, renal disease, neurosurgery, gastrointestinal problems, wound healing and nutrition, shock, pulmonary subjects and cardiovascular surgery. The papers are uniformly of high quality and, while highly specialized, the general topics covered are of interest to surgeons involved in surgical research. Most of the papers presented have important and direct application, which will make the volume of interest to many clinicians who are not actively engaged in research.

While this volume is most attractive not only in its content but in its production, it would, in this reviewer's opinion, have been improved by the inclusion of discussion which must have followed each of the presentations.

GASTROENTEROLOGIC MEDICINE. Edited by Moses Paulson. 1627 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1969. $66.00.

This encyclopedic text of modern thought about gastroenterology covers 1585 pages. There are 85 contributors, and the editor has done an admirable job of maintaining a standard of excellence which makes for easy reading. The balance between detailed description of common diseases and tests, together with brief reference to less common conditions, has been well struck. Most of the photographs are in black and white and the book suffers slightly from this. The tables and graphs are clear and concise. The list of references after each chapter is quite complete and contains key references.

This is an excellent reference text book that will be of interest to both students and practitioners. Its size, encyclopedic nature, and cost would make it impractical for those who are not specialists, but it should be in every medical library.

IMMUNOBIOLOGY FOR SURGEONS. J. Wesley Alexander and Robert A. Good. 220 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1970. $13.00.

A wealth of information on immunobiology of interest to surgeons is clearly presented in this well-organized little text. New advances are placed in perspective and interpreted in a way not possible in the original papers. The new basic science herein outlined has very practical application for the understanding and treatment of patients with cancer, infections and deficiency diseases, and in the management of those who require transfusions, transplants or drug therapy. These are but 6 of 14 chapter headings in this monograph concerned with the expanding field of immunobiology.

This timely volume introduces the topic with a discussion of non-specific immunity and the phylogeny of adaptive immunity. Particularly good is the chapter on mechanisms of immunologic injury which clarifies and analyzes the corresponding human diseases, associated with injury involving humoral, cell-mediated and non-specific immunity. A summary follows each chapter together with suggestions for further reading.

A new look is taken at many old problems that all surgeons will find interesting. The new laboratory techniques, the new nomenclature and the new approaches must be part of our future.

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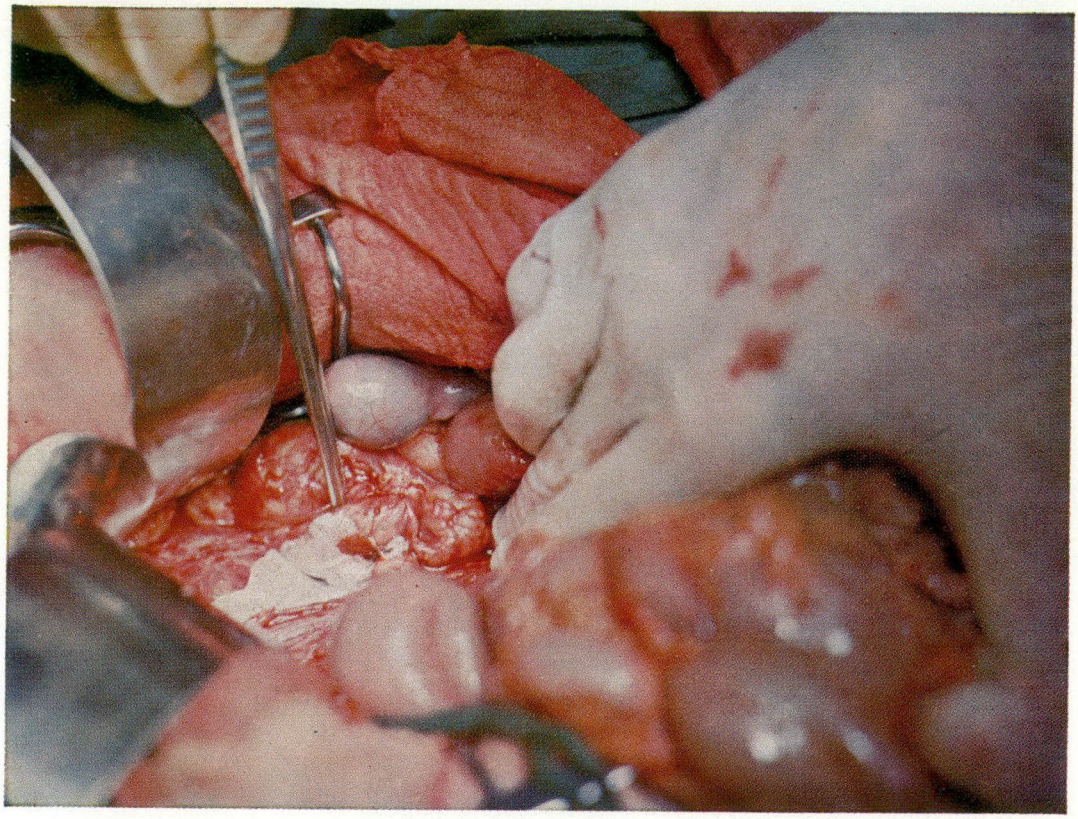

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INTERNATIONAL WORKSHOP ON ARTIFICIAL FINGER JOINTS. Proceedings of the First International Workshop held at the Royal Postgraduate Medical School, London, April 14th and 15th, 1969. Edited by J. S. Calnan and P. J. L. Holt. Supplement to Annals of the Rheumatic Diseases, vol. 28, no. 5. 109 pp. Illust. British Medical Association, London, 1969. 30/-. $3.75 (approx.). Paperbound.

On April 14 and 15, 1969 an international workshop was held at the Royal Postgraduate Medical School, London. The purpose of the meeting was to discuss artificial finger joints. It brought together the pioneers of finger-joint replacement such as Flatt, Swanson, Niebauer, Reis and Calnan. For the defence of excisional arthroplasty were those experienced campaigners Vaughan-Jackson and Savill. To keep both groups honest a number of rheumatologists and physiatrists were present.

Calnan and Holt have collected the papers read at this meeting and published them in a well-produced slim volume. The first papers cover the anatomy and pathology of the arthritic hand. A section on biomechanics follows and the various arthroplasties are described. The early state of the art is obvious from the opposing views of the surgeons on whether the prosthesis should be free to move within the bone, firmly or rigidly fixed. Reis and Calnan cement their device in place whereas Swanson insists on a loose fit for long life of the Silastic hinge. Opinions are similarly divided on the length of time external splints are required in the postoperative phase. Papers on assessment, surgical technique and present research complete the supplement.

Each section ends with the discussion that occurred. Some delightful exchanges forced participants to declare themselves as though under oath. More meetings of this kind and their published record would help greatly both education and the practice of medicine.

The reviewer strongly recommends this book to all who care for arthritic patients. It will help them to understand better the complexity of disturbed hand function in rheumatoid disorders and the maior effort presently being exerted in the rehabilitation of such hands.

LAW AND THE SURGICAL TEAM. Carl Erwin Wasmuth and Carl Erwin Wasmuth, Jr. 414 pp. The Williams & Wilkins Company, Baltimore; Burns & MacEachern Limited, Toronto, 1969. $14.85.

A reader of this book must be aware of a frequently used legal phrase "*res ipsa loquitur*" —the thing (fact) speaks for itself. In the early part of this book, which deals with many malpractice suits, it is the reader who must work to find the facts. It is evident that each

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suit depends on the responsibilities expected of the physician in his community.

There is much of value in this book for superintendents of hospitals, directors of teaching units, administrators of group practice, clinics or emergency hospital units and individual surgeons and physicians. It helps to delineate the responsibility of the hospital and its employees, the surgeon, anesthetists and others associated in a surgical team, and gives good advice in establishing the responsibility of each.

It deals with the problems of the changed hospital practice, and although based on American law it is equally applicable to Canadian hospital practice. It is pointed out, for example, that an insufficiently supervised medical student may be the cause of a negligence action against the hospital and staff and that he may also be charged with practising medicine without a licence. The foreign medical graduate's problems regarding licence and language in hospital practice are fully explored.

The changing attitude of the law to blood transfusions to members of the Jehovah's Witness is well described. It is apparent that in Canada and the United States there is freedom of religion but not necessarily the practice of that religion. A wife would be prevented from entering the funeral pyre of her husband. Should a mother of a 9-month-old child allow herself to die and rob the child of her care? Should a physician jeopardize his conscience and professional oath and legal position by rendering treatment less than the standard of that rendered in the community, by acceding to the restriction placed on him by a patient or his agent? In some jurisdictions in the United States the courts have ruled that individuals do not have the privilege of dying and have empowered physicians to render necessary treatment which may include blood transfusions.

This book shows that the surgeon is no longer "the captain of the ship" and responsible for the actions of his crew, but part of a team of physicians, nurses and technicians working in hospital, and outlines the responsibilities the law has found for each. However, because of the large number of judgments quoted verbatim, this is not an easy book to read.

LIVES OF THE FELLOWS OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND 1952-1964. R. H. O. B. Robinson and W. R. Le Fanu. 470 pp. E. & S. Livingstone Ltd., Edinburgh; The Macmillan Company of Canada Limited, Toronto, 1970. £6. $15.00 (approx.).

Those who have their surgical education roots in the United Kingdom, and those interested in British surgery and the men who have given it its distinctive flavour will welcome this fourth volume which includes brief biographies of those Fellows of the English College who died between 1952 and 1964. For reasons that are difficult to explain the present volume seems of greater interest and readability than the third volume which ran to almost twice as many pages. This may be owing to the fact that many lives recorded in this volume are "contemporary" in that the surgeons will be known personally to the reader or perhaps, as suggested by Sir Cecil Wakeley who writes the foreword, this volume is more personal and contains more about the social activities of the Fellows.

The biographies run from one-half to two pages and provide ample footnotes for those in search of additional information. The entries are remarkable for their candour. It is said of one distinguished surgeon that "He was a difficult man to serve since he was jealous of rivalry from his colleagues and overbearing to his officials." This is a well-written reference which will interest all who enjoy surgical history and biography.

PEDIATRIC SURGERY. Vols. 1 and 2. 2nd ed. Edited by William T. Mustard and others. 1575 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1969. $55.00.

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This second edition of "Pediatric Surgery" is considerably larger than the previous one because of the tremendous growth in the specialty of pediatric surgery since the first edition appeared in 1962. Many of the older chapters have been rewritten, and this work includes new chapters dealing with recent developments.

The general plan of the new edition is much the same as before; however, the list of contributors has been considerably increased. New chapters such as "Genetic Considerations in Disease" discuss single and multiple genetic inheritance, chromosomal abnormalities and transplantation problems. The chapter on anesthesiology now places greater stress on the use of non-explosive anesthetic agents. A chapter has been added dealing with the chemotherapy of solid tumours, and the battered child syndrome is also discussed.

Drugs and anti-bacterial agents now constitute a separate chapter because infection plays such an important role in preoperative and postoperative morbidity. An important addition is a comprehensive section dealing with disorders of the salivary glands.

The section on the physiological considerations of pulmonary and cardiac abnormalities has been considerably expanded to keep abreast of rapidly advancing knowledge.

The liver and biliary-tract section has been enlarged; an excellent discussion of tumours of the liver clearly outlines the surgical management of these tumours.

A new section discusses disorders of the clotting mechanism both in disease states and in hemorrhage associated with cardiopulmonary bypass.

The chapter on colon surgery has been expanded to include gastrointestinal polyps. The section on Hirschsprung's disease now describes several operative procedures for this abnormality.

The sections on the genitourinary system and the nervous system have been expanded to give a full discussion of abnormalities in these areas.

In summary, "Pediatric Surgery" is very comprehensive and should be of great value to the pediatric and general surgeon, and other doctors who have to make decisions regarding surgical conditions in infants and children.

ORTHOPAEDIC BIOMECHANICS. The Application of Engineering to the Musculoskeletal System. Victor H. Frankel and Albert H. Burstein. 188 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1970. $10.50.

This 188-page monograph is illustrated by numerous line drawings and black-and-white plates. Throughout, the text and illustrations are clear. The subjects dealt with are: statics and dynamics, elasticity, energy and work, viscoelasticity, kinematics, lubrication and design.

Every orthopedic surgeon and every orthopedic resident in training should have this book in his library because it deals clearly and concisely with engineering principles applied to the locomotor system. It will also prove useful to the physiotherapist, and to the engineering student who is interested in the locomotor system of man and other animals.

At present the average practitioner and student of orthopedic surgery often has slender knowledge of biomechanics and, quite rightly, this subject is assuming increasing importance in this specialty. In the orthopedic journals the student is now confronted with an increasing number of papers dealing with biomechanics. This concise textbook will give the orthopedic surgeon an excellent introduction to the subject and help him to understand the journals with much greater ease and effectiveness.

DIE THERAPIE DER KOXARTHROSE. Edited by August Rütt. 310 pp. Illust. Georg Thieme Verlag, Stuttgart, Germany, 1969. DM 78,00. $11.20 (approx.).

This book marks the seventy-fifth birthday of Matthias Hackenbroch who has made significant contributions to our understanding of coxarthrosis. He introduced the term "prearthrosis" to cover a disturbance of the hip joint such as a scar, a defect or a functional alteration which eventually led to arthrosis.

The treatment can be operative or nonoperative; the latter is recommended only in patients who either refuse or cannot tolerate an operation. Conservative treatment consists of reduction of the load on the hip joint and decrease of motion with appropriate braces. Physical medicine and drugs have a definite but limited place in the treatment.

The main portion of the book is devoted to a discussion of the operative treatment of coxarthrosis. Chapters by different authors describe and discuss the various types of osteotomy, arthroplasty, muscle release operation and the insertion of endoprostheses.

The monograph does not offer many new facts to the orthopedic surgeon, but may draw his attention to different schools of thought. For other clinicians, it is an excellent summary of the various theories and practices in use at the present time. Some chapters are in English, but most are in German.

Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Acrylic Cement in Orthopaedic Surgery. John Charnley. 131 pp. Illust. E. & S. Livingstone Ltd., Edinburgh; The Macmillan Company of Canada Limited, Toronto, 1970. $9.75.

Advances in Surgery. Vol. 4. Edited by Claude E. Welch. 413 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1970. $17.50 (approx.).

After Vagotomy. Edited by J. Alexander Williams and Alan G. Cox. 433 pp. Illust. Butterworth & Co. (Publishers) Ltd., London; Butterworth & Co. (Canada) Ltd., Toronto, 1969. $18.25.

Akute Chirurgische Erkrankungen. Notfallfibel zur Diagnose und Therapie. Richard X. Zittel and Walter E. Zimmerman. 201 pp. Illust. Georg Thieme Verlag, Stuttgart, Germany, 1970. DM 29,80. $8.50 (approx.). Paperbound.

An Atlas of Children's Surgery. Robert E. Gross. 191 pp. Illust. W. B. Saunders Company Canada Limited, Toronto, 1970. $20.55.

Atlas of the Human Brain in Section. Melville Roberts and Joseph Hanaway. 95 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1970. $9.65.

Cardiovascular Pathology. Vol. 3. Supplement to Vols. 1 & 2. Reginald E. B. Hudson. 1166 pp. Illust. Edward Arnold (Publishers) Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1970. $78.50.

Chemotherapy of Cancer. Edited by Warren H. Cole. 349 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1970. $13.75.

Clinical Orthopaedics and Related Research. Number Sixty-Seven. Sponsored by the Association of Bone and Joint Surgeons. Editor-in-Chief: Marshall R. Urist. 264 pp. Illust. J. B. Lippincott Company, Philadelphia; J. B. Lippincott Company of Canada Ltd., Toronto, 1969. $10.00.

Facial Injuries. Richard Carlton Schultz. 264 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1970. $15.00.

Functional Pathology of the Human Adrenal Gland. Thomas Symington. 551 pp. Illust. E. & S. Livingstone Ltd., Edinburgh; The Macmillan Company of Canada Limited, Toronto, 1969. $32.75.

Gastroenterologic Medicine. Edited by Moses Paulson. 1627 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1969. $66.00.

General Anesthesia and the Central Nervous System. A Basic Science and Clinical Consideration. Leonard C. Jenkins. 544 pp. Illust. The Williams & Wilkins Co., Baltimore; Burns & MacEachern Ltd., Toronto, 1969. $19.25.

Injuries of the Knee Joint. 4th ed. I. S. Smillie. 393 pp. Illust. E. & S. Livingstone, Edinburgh; The Macmillan Company of Canada Limited, Toronto, 1970. $25.75.

The Intersexual Disorders. Christopher J. Dewhurst and Ronald R. Gordon. 154 pp. Illust. Baillière, Tindall and Cassell Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1969. $8.50.

Modern Surgery. Richard H. Egdahl and John A. Mannick. 1194 pp. Illust. Grune & Stratton, Inc., New York; Longmans Canada Limited, Toronto, 1970. $22.75.

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